UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ABBOTT GMBH & CO., KG; ABBOTT BIORESEARCH CENTER, INC.; and ABBOTT BIOTECHNOLOGY LTD.,	)	
Plaintiffs,	)	**Civil Action No. 09-11340-FDS**
v.	)	
CENTOCOR ORTHO BIOTECH, INC., and CENTOCOR BIOLOGICS, INC.	)	
Defendants.	)	

MEMORANDUM AND ORDER ON
CROSS-MOTIONS FOR SUMMARY JUDGMENT

SAYLOR, J.

This is a patent infringement action involving a class of antibodies developed to treat certain auto-immune diseases. Plaintiffs Abbott GmbH & Co., KG; Abbott Bioresearch Center, Inc.; and Abbott Biotechnology Ltd. (collectively "Abbott") and defendants Centocor Ortho Biotech, Inc and Centocor Biologics, Inc. (collectively "Centocor") are pharmaceutical companies. Abbott and Centocor have both developed antibodies capable of treating diseases associated with the overproduction of a naturally-occurring protein in the human body called interleukin-12 ("IL-12"). Abbott seeks a judgment under 35 U.S.C. § 271 that its U.S. Patent No. 6,914,128 (the "'128 patent") and U.S. Patent No. 7,504,485 (the "'485 patent") are infringed by the drug Stelara, which Centocor manufactures. Centocor seeks declarations that Stelara does not infringe the patents and that the patents are invalid under 35 U.S.C. §§ 102, 103, and 112.

The parties are simultaneously before this Court on an appeal of a decision of the United States Patent and Trademark Office ("PTO") Board of Patent Appeals and Interferences ("BPAI") regarding essentially the same subject matter. On December 12, 2007, the BPAI declared an interference between Abbott's '128 patent and Centocor's pending Patent Application No. 10/912,994 for Stelara. That proceeding was instituted to determine priority of invention as between the parties and whether the '128 patent claimed material that was unpatentable under 35 U.S.C. §§ 102, 103, and 112. On August 6, 2009, the BPAI ruled for Abbott on these issues. Centocor has petitioned for judicial review of the interference decision pursuant to 35 U.S.C. § 146.

This Court conducted a *Markman* hearing in the infringement action and issued its final claim construction decision on May 5, 2011. The parties have now filed multiple cross-motions for summary judgment on the issues of validity and infringement.[1]

I. Background

This case concerns the interrelation of two statutory causes of action as well as questions of infringement involving application of the claim construction to technical subject matter. A brief review of the relevant statutory, factual, and procedural background is therefore warranted.

A. Statutory Background

1. Infringement Actions Under 35 U.S.C. § 271

Two statutes, 35 U.S.C. § 271 and 281, provide a patentee with a cause of action for

[1] On September 16, 2011, President Obama signed the Leahy-Smith America Invents Act., Pub. L. No. 112-29, 125 Stat. 285 (2011). Section 35 of the Act provides that, subject to certain exceptions, "the provisions of this Act shall take effect upon the expiration of the 1-year period beginning on the date of the enactment of this Act and shall apply to any patent issued on or after that effective date." *Id.* § 35, 125 Stat. at 341. The Act therefore does not alter the law applicable to this action.

damages and injunctive relief for patent infringement. Infringement analysis is a "two-step process in which the court first determines, as a matter of law, the correct claim scope, and then the fact-finder compares the properly construed claim to the accused device to determine, as a matter of fact, whether all of the claim limitations are present, either literally or by a substantial equivalent in the accused device." *IEX Corp. v. Blue Pumpkin Software, Inc.*, 122 Fed. Appx. 458, 464 (Fed. Cir. 2005).

Because "an invalid patent cannot be infringed," *Viskase Corp. v. American Nat'l Can Co.*, 261 F.3d 1316, 1323 (Fed. Cir. 2001), a defendant in an infringement action may assert invalidity as an affirmative defense. However, a granted patent is "presumed valid," 35 U.S.C. § 282, and this presumption may be rebutted only by "clear and convincing evidence." *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2242 (2011); *see also Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986) (holding that "the clear-and-convincing standard of proof should be taken into account in ruling on summary judgment motions").

2. <u>Interference Proceedings and Judicial Review Under 35 U.S.C. § 146</u>

The Director of the PTO is authorized to declare and conduct interference proceedings by 35 U.S.C. § 135. The statute provides, in relevant part:

> Whenever an application is made for a patent which, in the opinion of the Director, would interfere with any pending application, or with any unexpired patent, an interference may be declared . . . . The [BPAI] shall determine questions of priority of the inventions and may determine questions of patentability. Any final decision, if adverse to the claim of an applicant, shall constitute the final refusal by the [PTO] of the claims involved, and the Director may issue a patent to the applicant who is adjudged the prior inventor. . . .

35 U.S.C. § 135(a).[2] At the beginning of an interference, the BPAI defines one or more "counts." 37 C.F.R. § 41.203(b). A count is "the Board's description of the interfering subject matter that sets the scope of admissible proofs on priority." 37 C.F.R. § 41.201. It "corresponds to a patentable invention" and "may be identical to a single claim at issue or may be broader than the particular claims at issue." *Slip Track Sys., Inc. v. Metal-Lite, Inc.*, 304 F.3d 1256, 1263 (Fed. Cir. 2002). The party that was first to file an application describing and enabling the "count" declared in the interference is designated the "senior party," and the second the "junior party." The junior party bears the burden of proving priority by a preponderance of the evidence. 37 C.F.R. § 41.207(a); *Rexam Indus. Corp. v. Eastman Kodak Co.*, 30 Fed. Appx. 983, 985 (Fed. Cir. 2002).

Once an interference is properly declared, a priority determination is mandatory. *See Guinn v. Kopf*, 96 F.3d 1419, 1421-22 (Fed. Cir. 1996). A patentability determination, if fairly raised and fully developed before the BPAI, is "nearly mandatory." *In re Gartside*, 203 F.3d 1305, 1317 (Fed. Cir. 2000); *see also Perkins v. Kwon*, 886 F.2d 325, 328-29 (Fed. Cir. 1989) (interpreting the phrase "may determine questions of patentability" to require a determination unless patentability is not placed at issue); *Koninklijke Philips Elecs. N.V. v. Cardiac Sci. Operating Co.*, 590 F.3d 1326, 1334 (Fed. Cir. 2010) (citing *Perkins*, 886 F.2d at 328).

Once the BPAI has rendered a final decision, Section 146 of the Patent Act authorizes an aggrieved party to seek review of that decision in federal district court. The statute provides:

> Any party to an interference dissatisfied with the decision of the [BPAI] on the interference, may have remedy by civil action . . . . Such suit may be instituted

[2] For a detailed discussion of the BPAI interference process, *see Human Genome Scis., Inc. v. Amgen, Inc.*, 552 F. Supp. 2d 466, 467 (D. Del. 2008).

> against the party in interest as shown by the records of the [PTO] at the time of the decision complained of, but any party in interest may become a party to the action. . . . Judgment of the court in favor of the right of an applicant to a patent shall authorize the Director to issue such patent on the filing in the [PTO] of a certified copy of the judgment and on compliance with the requirements of law.

35 U.S.C. § 146. "District court review of an interference proceeding under Section 146 is an equitable remedy of long standing." *General Instrument Corp. v. Scientific-Atlanta, Inc.*, 995 F.2d 209, 214 (Fed. Cir. 1993).

An action in district court pursuant to Section 146 takes the form of a "hybrid appeal/trial *de novo* proceeding in which the PTO record is admitted on motion of either party [but] may be supplemented by further testimony." *Human Genome*, 552 F. Supp. 2d at 468 (quoting *General Instrument*, 995 F.2d at 212). To the extent that no new evidence is presented in the Section 146 action, the district court reviews the factual findings of the BPAI for "substantial evidence," the standard applicable to review of agency fact-finding under the Administrative Procedure Act. *Dickinson v. Zurko*, 527 U.S. 150, 152 (1999). However, if the parties do introduce new evidence in the form of live testimony before the district court, its review of the BPAI's determinations is *de novo*. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 1345 (Fed. Cir. 2000). Although it has some aspects of a trial, a Section 146 action "is not a new claim, but an authorized phase of the interference proceeding that is conducted by the PTO and is subject to judicial review." *Vas-Cath, Inc. v. Curators of the Univ. of Mo.*, 473 F.3d 1376, 1382 (Fed. Cir. 2007); *Rexam Indus. Corp. v. Eastman Kodak Co.*, 182 F.3d 1366, 1370 (Fed. Cir. 1999) (stating that a Section 146 action is "derivative of the interference conducted in the PTO.").

B. Factual Background

The following facts are undisputed except where otherwise noted.

1. Human IL-12 and Recombinant Antibodies to It

IL-12 is a member of a family of naturally occurring human proteins, called cytokines. It assists the immune system by binding to receptors on the surfaces of certain cells as part of the body's inflammation response to infection. Structurally, IL-12 is composed of two smaller molecules, a p35 subunit and a p40 subunit.[3]

In some individuals, the body can over-produce IL-12, causing auto-immune diseases such as psoriasis, where the body's immune system chronically targets healthy human tissue instead of foreign contaminants. One way of treating such diseases is by inhibiting or blocking the effects of IL-12 through the use of antibodies. Antibodies are proteins that attach themselves to a target molecule—called an "antigen" for that antibody—by binding with a portion of that antigen called an "epitope." The immune system produces antibodies that typically target antigens such as viruses, foreign bacteria, or other foreign substances, but an antibody may also target a non-foreign antigen such as IL-12.

The ability of an antibody to bind to a specific antigen is determined by its molecular structure. All antibodies share a general structure consisting of two identical "heavy" chains and two identical "light" chains that are joined together in a "Y" shape. Some portions of these protein chains are constant, meaning that the same sequences of amino acids appear in all antibodies. Other segments vary, but are constant for all antibodies of a given animal species, allowing the immune system of that species to distinguish its own antibodies as from foreign substances. Finally, certain portions of those segments that appear at the tips of the "Y" vary in

[3] The notation used to describe these subunits indicates their molecular mass. Thus, the p35 subunit of IL-12 has a molecular mass of thirty-five kilodaltons, while the p40 subunit has a mass of forty kilodaltons.

each antibody. These areas—known as Complementarity Determining Regions ("CDRs")—determine whether, and how effectively, an antibody will bind to a given antigen.

The immune system naturally develops antibodies as a response to a foreign antigens in the body. A class of white blood cells called B cells assemble the DNA sequences that encode those antibodies out of component antibody genes. These component genes are germline DNA sequences, meaning that they are part of the person's DNA that is inherited from his or her parents. The B cells produce a large variety of antibodies from a limited pool of germline antibody genes by splicing and rearranging those genes in a process called recombination. Further antibody diversity is achieved through a process called N-nucleotide addition. N-nucleotides are short segments of DNA that is "non-template," meaning that it is not part of any germline DNA sequence. In N-nucleotide addition, individual N-nucleotides are added at the junctions where the segments of spliced antibody genes are rejoined. This assembly and mutation process adds variation to the DNA that encodes the variable regions of antibodies, allowing the creation of a large array of antibodies with unique binding properties. B cells that assemble effective antibodies then proliferate and produce more antibodies; by binding to their target, these antibodies allow the immune system to destroy or remove it from the body.

Because, however, IL-12 is a non-foreign, human protein, the immune system does not naturally produce antibodies against it. Treatment of the over-production of IL-12 therefore requires the artificial creation of such antibodies. The subject matter of Abbott's '128 and '485 patents is a set of antibodies for IL-12 developed through genetic engineering techniques. Likewise, Stelara contains an antibody developed by Centocor that, while structurally distinct from the antibodies described in Abbott's patents, also targets human IL-12.

2. Methods for Engineering Antibodies for IL-12

To be safe and effective as a treatment for the overproduction of a human antigen like IL-12, an antibody must share certain general characteristics with naturally-occurring human antibodies. If it does not, the antibody may be recognized by the body as foreign and thereby itself become the target of a potentially dangerous immune response.[4] Although several methods exist for developing artificially engineered antibodies to a human antigens, not all methods result in "human" antibodies that are safe for treatment.

An early method for artificially creating an antibody to a human antigen was to inject the antigen into a non-human species, typically a mouse. B cells in the mouse would then develop antibodies to what the mouse's immune system perceived as a foreign antigen. An antibody produced in this way is not human, but murine, and so it has limited usefulness for treatment. An alternative method is to create a "chimeric antibody" by taking a non-human antibody that has variable regions capable of targeting the human antigen and then substituting a human constant region into that antibody. Chimeric antibodies are less likely to be recognized as foreign by a patient's body; the risk of an adverse reaction to treatment is therefore lower. Another method is to create a "humanized antibody" by grafting human DNA that encodes the antibody's constant regions onto murine genes corresponding to its CDRs. A humanized antibody exhibits the desired binding characteristics while containing minimal amounts of non-human genes in its DNA. Nonetheless, because it does contain some murine variable regions, a humanized antibody is not

[4] When this response results from the introduction of antibodies developed by the immune system of a mouse, it is known as a Human Anti-Mouse Antibody ("HAMA") response. HAMA responses reduce the effectiveness of the antibody treatment as the immune system removes the antibody from the patient's circulation. The allergic reaction produced during a HAMA response can be life-threatening.

fully human and does not eliminate the risk of adverse responses in human patients.

Two technologies allow the development of "fully human" antibodies that target human antigens with minimal risk of triggering adverse immune reactions. The first method, phage display technology, involves the use of bacteria that have been transfected with viral DNA that contains DNA corresponding to human antibody variable regions. The bacteria create viruses that have those variable regions expressed as proteins on their surfaces. The viruses that display antibody proteins with desired binding properties are screened (or "panned") by bringing them in contact with the target antigen and removing those that bind to it. The DNA encoding the corresponding antibody is then isolated and replicated. An antibody produced by this method is "recombinant," meaning that it is created by splicing and recombining DNA.

The second method for producing human antibodies harnesses the immune system of a transgenic mouse.[5] In a transgenic mouse, some of the genes that encode its antibodies have been replaced with human antibody genes. When a human antigen such as IL-12 is introduced into a transgenic mouse, the animal's immune system may recognize the antigen as foreign and develop antibodies that target it. If the mouse's B cells assemble an antibody using the human antibody genes substituted into the mouse's DNA, the resulting antibodies will correspond primarily to that human germline DNA. As in human B cells, however, some alterations to that DNA will occur through N-nucleotide addition in the assembly process. Nonetheless, because the genes from which the transgenic animal's B cells build the antibody are human, the resulting antibody will be

[5] Centocor argues that the antibody contained in Stelara is not a "human antibody" within the meaning of this court's claim construction, even if it is fully human as the term is used here (that is, to indicate that an antibody is non-immunogenic in humans). (Pearson Ex. 64, '734 Patent col. 6 ll. 46-50; Centocor Mem. Supp. # 2, at 1).

unlikely to trigger adverse immune responses in human patients. Antibodies with desired binding properties can then be reproduced using what is known as the hybridoma technique, by which B cells producing those antibodies are harvested from the spleen of the transgenic mouse and fused to cancer-cell lines that, when grown in culture, secrete the antibodies.

3. Binding and Neutralizing Properties of Antibodies

To be effective in treating diseases caused by over-produced IL-12, an antibody produced by the methods previously described must possess several characteristics. One such characteristic is "specificity" to IL-12. An antibody is highly specific to an antigen if it attaches only to that antigen. An antibody with low specificity can be less effective because some of the antibody attaches to other substances, reducing the amount available to neutralize the target antigen and potentially causing unwanted side effects.

Two other desirable characteristics of an antibody are "affinity" and "neutralizing" ability. "Affinity" is the strength with which an antibody binds, or attaches, to a target antigen. "Neutralizing" ability is the capability of that antibody to inhibit one or more biological activities of the antigen to which it binds. Although high affinity is commonly associated with neutralizing ability, an antibody may have high affinity but be non-neutralizing.

One measure of affinity is the dissociation constant, or "K_d" value, of the antibody-antigen interaction. Antibody-antigen interactions are dynamic, and the ongoing association and dissociation of antibodies and antigens is measured in terms of kinetic rate constants. The rate at which antibodies detach from the target antigen is commonly referred to as "k_{off}," while the rate at which they attach to that antigen is the "k_{on}" value of the interaction. K_d is calculated from measurements of the rate constants according to the formula $K_d = k_{off} / k_{on}$. This ratio describes

the overall binding affinity of the antibody and antigen.

The k_{on} and k_{off} values of an antibody-antigen interaction may be measured using an optical phenomenon called surface plasmon resonance ("SPR"). SPR testing can be conducted using a BIAcore instrument, which consists of a light source, a sensor chip with a gold film, a flow channel, and an optical detection unit. To test the interaction of an antibody and antigen, the antibody is immobilized on the sensor chip surface while a solution containing the antigen is passed over the chip through the flow channel.[6] As the antigen binds and dissociates from the immobilized antibody, optical SPR changes occur and are measured by the detector. From these data, the experimenter can calculate k_{on} and k_{off} values for the interaction.

Accurate measurement of binding properties using SPR requires appropriate test conditions. These conditions are controlled by adjusting certain experimental conditions. Two such parameters are "flow rate" and "antibody surface density." Flow rate, the rate at which the antigen solution is passed over the sensor surface, is measured in micro-liters per minute (μl/min). Antibody surface density, which refers to the amount of immobilized antibody on the sensor chip surface, is measured in "resonance units" ("RUs").

The neutralizing ability of an antibody can be measured in terms of its "IC_{50}" value, the concentration of that antibody required to cut the biological activity of the target antigen in half. One method for determining the IC_{50} of an antibody to IL-12 that is particularly relevant here is the receptor-binding assay ("RBA"). RBAs rely on the knowledge that IL-12 binds to certain receptor proteins to test the ability of an antibody to prevent IL-12 from binding to those

[6] In these experiments, the substance that is attached to the sensor surface is called the "ligand," while the substance that is passed over the surface is known as the "analyte."

receptors. By measuring the amount of such binding in the presence and absence of an antibody, a scientist can determine the IC_{50} for that antibody as a neutralizing agent for IL-12.

4. Development of IL-12 Antibodies by Abbott

The IL-12 antibodies described in the '128 and '485 patents were developed using phage display technology in a collaboration of three separate companies: BASF BioResearch Corporation (a predecessor to Abbott, which for the sake of convenience will be referred to as "Abbott"), Genetics Institute ("GI"), and Cambridge Antibody Technology ("CAT").

During a meeting on July 13, 1993, three Abbott scientists—Drs. Salfeld, Tracey, and Banerjee—suggested antibodies that specifically bind to IL-12 as a potential target for research. A memorandum was circulated identifying these antibodies as a research priority. In August 1993, Abbott entered into a research agreement with CAT for the development of antibodies to human antigens.[7] In 1995, GI joined the partnership specifically for the purpose of developing an antigen to IL-12. At least 22 scientists employed by the three companies would eventually be named as inventors on the patents that resulted from the IL-12 project.

In late 1995 and early 1996, researchers working on the project identified several antibodies with the ability to bind to IL-12. These antibodies, known as the Joe 7, 9, and 10 antibodies, respectively, were subsequently used to develop antibodies for IL-12 with higher affinity and neutralizing effect. Laboratory manipulation of the amino-acid sequences of Joe 9 eventually yielded an antibody called Y61, which had substantially improved ability to bind to and neutralize IL-12. Further experimentation led to the discovery of an antibody known as J695,

[7] The parties do dispute the scope, effect, and effective date of certain agreements that the three companies entered into during this period.

which binds to and neutralizes IL-12 to a degree that makes it effective for treatment.

On March 25, 1999, Abbott filed a provisional application for a patent on human antibodies that specifically bind to human IL-12. On March 24, 2000, it filed a related application, U.S. Patent Application 09/534,717, that described 50 antibodies that bind to an epitope located on the p40 subunit of IL-12. The application set forth 74 claims covering antibodies that share with the disclosed antibodies particular binding properties in relation to IL-12. The PTO granted the application as the '128 patent on July 5, 2005.

At some time during the development of the antibodies for IL-12 disclosed in the '128 patent, Abbott became aware that those antibodies also bind to another human cytokine, interleukin-23 ("IL-23").[8] IL-23 contains the same p40 subunit that exists in IL-12, but with a p19 subunit forming its second half instead of the p35 subunit contained in IL-12. Some of the disclosed antibodies that bind to an epitope located on the p40 subunit of IL-12 also bind to that subunit of IL-23.

On July 1, 2004, Abbott filed U.S. Patent Application 10/884,830 as a divisional of the 09/534,717 application. The new application claimed antibodies that bind to the p40 subunit of IL-12 both when it binds to a p35 subunit to form IL-12 and when it binds to a p19 subunit to form IL-23. Abbott amended the application on January 4, 2007, and the PTO granted the amended application as the '485 patent on March 17, 2009.

Abbott currently has an antibody product within the scope of its patents called ABT-874,

[8] The parties dispute when IL-23 became known in the art and when Abbott became aware and could adequately describe the similarities between IL-12 and IL-23 that allow the disclosed antibodies to bind to the second antigen. (Pearson Ex. 17, Siegel Rpt. ¶¶ 39, 42; Oyloe Ex. 123, Tracey Dep. Tr. at 161-62; Oyloe Ex. 78, Marks Rebuttal Rpt. ¶ 456).

or briakinumab. The drug, which treats psoriasis and other diseases by targeting IL-12 and IL-23, is in late-stage clinical trials.

5. Development of Stelara

In approximately March 1997, Centocor scientists, under the direction of Jill Giles-Komar, began work on developing a fully human neutralizing antibody to IL-12 using transgenic mouse technology. On September 4, 1997, one scientist on the team identified a hybridoma that produced an antibody that binds to IL-12; that antibody was later named ustekinumab.[9] By February 25, 1998, Centocor scientists had created a pharmaceutical composition of ustekinumab. No later than April 30, 1998, Ms. Giles-Komas confirmed that the antibody had the desired binding and neutralizing characteristics. Like J695 and other antibodies described in the '128 and '485 patents, ustekinumab binds to the p40 subunit of IL-12.

Further experimentation on ustekinumab followed. On August 7 and September 29, 2000, Centocor filed provisional patent applications claiming human, neutralizing antibodies to IL-12. It filed a non-provisional application on the subject matter on August 1, 2001. On August 6, 2004, it filed U.S. Patent Application 10/912,994 as a divisional of the 2001 application.

Centocor has since developed Stelara, a drug based on ustekinumab that Abbott contends infringes its patents. Stelara has received FDA approval for use in the United States.

C. Procedural Background

On December 12, 2007, the BPAI declared an interference between Abbott's '128 patent and Centocor's still-pending U.S. Patent Application 10/912,994. It instituted a proceeding to determine priority under Section 102(g), obviousness under Section 103, and patent validity under

[9] Ustekinumab is also known as CNTO-1275.

the written description, enablement, and definiteness requirements of Section 112. The interference included a single count, which the PTO defined as "[a]n isolated human antibody according to claim 1 of U.S. Application 10/912,994 or claim 1 of U.S. Patent 6,914,128." (Oyloe Ex. 21, Interference Declr. at 5).[10] Claim 1 of the '994 application claimed an "isolated mammalian anti-IL-12 antibody," while claim 1 of the '128 patent claimed an "isolated human antibody . . . that binds to human IL-12." On August 6, 2009, the PTO Board ruled for Abbott on all issues raised in the interference.

On August 10, 2009, Abbott filed suit against Centocor in this Court, alleging that the sale of Stelara infringed upon the '128 and '485 patents. On August 28, 2009, Centocor instituted actions in the District Court for the District of Columbia challenging the PTO Board's ruling pursuant to 35 U.S.C. § 146 and seeking declarations of non-infringement and invalidity of Abbott's '128 and '485 patents. In accordance with the "first-filed" rule, this Court denied Centocor's motion to transfer the infringement action to the District of Columbia, while that court granted Abbott's motion to transfer the Section 146 and declaratory judgment proceedings here. This Court then consolidated the infringement and declaratory judgment actions for all purposes and consolidated all three actions for purposes of discovery.

After conducting a *Markman* hearing with respect to the construction of the relevant claims, this Court issued its original claim construction order on March 15, 2011.[11]

The parties have now filed multiple cross-motions for summary judgment. The first set of

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[10] The declaration stated that the claims in the '128 patent that corresponded to the count were 1-15, 27-40, and 50-64. (Oyloe Ex. 21, Interference Declr. at 5).

[11] That order was amended to correct an error on March 17 and again on May 5 to incorporate Centocor's request to include an additional term as part of the claim construction.

motions concerns Centocor's contention that the claims in Abbott's patents that are asserted against it are invalid. The second set addresses whether Stelara infringes the asserted claims of the patents.

III. Standard of Review

Summary judgment is appropriate when the pleadings, the discovery and disclosure materials on file, and any affidavits show that "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). "Essentially, Rule 56[] mandates the entry of summary judgment 'against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial.'" *Coll v. PB Diagnostic Sys.*, 50 F.3d 1115, 1121 (1st Cir. 1995) (quoting *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986)). In making that determination, the Court views "the record in the light most favorable to the nonmovant, drawing reasonable inferences in his favor." *Noonan v. Staples, Inc.*, 556 F.3d 20, 25 (1st Cir. 2009).

"Cross motions for summary judgment neither alter the basic Rule 56 standard, nor warrant the grant of summary judgment *per se*. Cross motions simply require us to determine whether either of the parties deserves judgment as a matter of law on facts that are not disputed. As always, we resolve all factual disputes and any competing, rational inferences in the light most favorable to the party against whom summary judgment has entered." *Wightman v. Springfield Terminal Ry.*, 100 F.3d 228, 230 (1st Cir. 1996) (internal citations omitted).

IV. Analysis

After this Court issued its claim construction decision, the parties filed twelve motions, which are summarized in the following table:

Plaintiffs' Motion	**Defendants' Motion**	**Subject Matter**
Summary Judgment Motion # 2: that defendants are collaterally estopped from alleging invalidity of the '128 patent		Whether the BPAI interference precludes raising validity issues in this action
Summary Judgment Motion # 3: that claim limitations relating to surface plasmon resonance are not indefinite	Summary Judgment Motion # 1: that the K_d claims are indefinite	Validity of '128 and '485 patents under 35 U.S.C. § 112, ¶ 2
	Summary Judgment Motion # 7: that all asserted claims lack written description	Validity of '128 and '485 patents under 35 U.S.C. § 112, ¶ 1
	Summary Judgment Motion # 3: that the p19 claims lack written description	Validity of the '485 patent under 35 U.S.C. § 112, ¶ 1
Summary Judgment Motion # 4: that the named inventors' own work is not "secret prior art"	Summary Judgment Motion #5: that the Joe antibodies qualify as prior art	Validity of '128 and '485 patents under 35 U.S.C. § 102(f) and (g)(2)
	Summary Judgment Motion # 6: that Stelara anticipated all asserted claims and/or composition claims	Validity of '128 and '485 patents under 35 U.S.C. § 102(g)(2)
Summary Judgment Motion # 1: infringement of k_{off} claims	Summary Judgment Motion # 2: non-infringement of all asserted claims	Whether Stelara infringes the '128 and '485 patents
	Summary Judgment Motion # 1: non-infringement of K_d claims	Whether Stelara infringes the '128 and '485 patents
	Summary Judgment Motion # 4: non-infringement of receptor binding assay claims	Whether Stelara infringes the '128 patent
Motion *in limine* to Exclude MACE Evidence		Whether evidence is admissible at trial

The Court will address these motions in the order presented above.

A. Issue Preclusion[12]

Abbott contends that Centocor is precluded from raising invalidity of the '128 patent as a defense in this action because it raised invalidity of the patent during the interference proceeding and lost. In alternative, Abbott contends that Centocor is at least barred from raising the specific arguments for invalidity that it made before the BPAI.[13]

Under the doctrine of issue preclusion, the decision of one tribunal precludes re-litigation of the same issue in a subsequent lawsuit if "(1) the issue sought to be precluded in the later action is the same as that involved in the earlier action; (2) the issue was actually litigated; (3) the issue was determined by a valid and binding final judgment; and (4) the determination of the issue was essential to the judgment." *Ramallo Bros. Printing, Inc. v. El Dia, Inc.*, 490 F.3d 86, 90 (1st Cir. 2007).[14]

In patent actions, courts have held that issue preclusion bars a litigant in an infringement action from raising issues that it has previously litigated and lost in another infringement action. In *Blonder-Tongue Labs., Inc. v. University of Ill. Found.*, 402 U.S. 313, 332-33 (1971), the Supreme Court established that the doctrine of non-mutual estoppel bars a patentee in an

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[12] Issue preclusion is also referred to as collateral estoppel, a synonymous term.

[13] Centocor argues that Abbott waived the defense of issue preclusion by failing to plead it in its answer. This position may have merit. *See* Fed. R. Civ. P. 8(c) ("[A] party must affirmatively state any . . . affirmative defense, including: . . . res judicata."); *Jones v. District of Columbia Dept. of Corr.*, 429 F.3d 276, 279 (D.C. Cir. 2005) (reversing lower court's grant of summary judgment based on an affirmative defense that was not pleaded). On the other hand, concern for judicial efficiency may justify a district court in dismissing a case *sua sponte*, on unpleaded *res judicata* grounds. *Krepps v. Reiner*, 377 Fed. Appx. 65, 67 (2d Cir. 2010). Because the Court ultimately finds issue preclusion inapplicable, resolution of this issue is unnecessary.

[14] Although substantive questions of patent law are within the exclusive jurisdiction of the Federal Circuit, issue preclusion is governed by regional circuit law. *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Contractors USA, Inc.*, 617 F.3d 1296, 1311 (Fed. Cir. 2010).

infringement action from asserting patent claims that were held invalid in a previous infringement action against a different defendant.[15] Conversely, a decision upholding the validity of a patent in one infringement action bars the same defendant from challenging validity of the same patent in a subsequent infringement action. *See Pall Corp. v. Fisher Scientific Co.*, 962 F. Supp. 210, 214 (D. Mass. 1997).[16]

These applications of issue preclusion are relatively straightforward, because the cases in which they apply involve only the effect of the decision in one infringement action on another subsequent infringement action. This case presents a more complicated situation. The validity issues that Centocor raised in this infringement action have previously been litigated not in another infringement action, but in a BPAI interference proceeding. Moreover, the same issues are simultaneously implicated in the concurrently pending Section 146 action in which Centocor is appealing the decision of the BPAI. The question before this Court is therefore how issue preclusion should operate in this unique procedural posture.

In its original briefs, Abbott argued only that Centocor was precluded from asserting invalidity by the BPAI decision. In response to the Court's request for further briefing on the significance of the pending Section 146 action, it has also asserted that the Section 146

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[15] This rule applies to prior determinations of unenforceability issues as well. *General Electro Music Corp. v. Samick Music Corp.*, 19 F.3d 1405, 1413 (Fed. Cir. 1994) ("The principle of *Blonder-Tongue* . . . respecting collateral estoppel also applies to unenforceability.").

[16] Abbott correctly argues that where consideration of validity is precluded by a previous decision, that preclusion extends to the entire issue of validity, and not just to individual arguments. *Meritor Transmission Corp. v. Eaton Corp.*, 2006 WL 3951711, at *7 (W.D.N.C. Sept. 26, 2006); *William T. Burnett*, 203 U.S.P.Q. 801, 803 (4th Cir. 1979) (quoting *Daniels v. Coe*, 116 F.2d 941, 943 (D.C. Cir. 1940)).

proceeding may also have preclusive effect in this action.[17] This memorandum will address the preclusive effect of each proceeding in turn.

1. BPAI Interference Decision

The Patent Act's unusual conglomeration of administrative and judicial processes in the adjudication of patent validity complicates the applicability of the doctrine of issue preclusion in this case. The BPAI's status as an administrative agency alone does not prevent its decision from precluding certain issues in this action; a judgment by an agency can have preclusive effect in subsequent lawsuits if the parties had a "full and fair opportunity to litigate" and the agency rendered the decision while acting in a "judicial capacity." *United States v. Utah Constr. & Min. Co.*, 384 U.S. 394, 422 (1966). When this is true, the agency judgment will ordinarily have preclusive effect, provided that the prerequisites for preclusion outlined in *Ramallo* are present. *Global NAPs, Inc. v. Massachusetts Dep't of Telecomm. & Energy*, 427 F.3d 34, 44 (1st Cir. 2005) (stating, in dicta, that requirements for preclusion were not present in an administrative action, but ruling on other grounds); *Aunyx Corp. v. Canon U.S.A., Inc.*, 978 F.2d 3, 7 (1st Cir. 1992) (applying requirements for issue preclusion to find that an agency decision did have preclusive effect).

The Court finds that, in the procedural posture of this lawsuit, the BPAI decision does not meet the third *Ramallo* requirement because it is not yet a "binding final judgment." *Ramallo*, 490 F.3d at 90. Whether a decision is sufficiently final to warrant preclusive effect turns on whether the parties had a "full and fair opportunity to litigate a matter," such that "the litigation of

[17] In its request for further briefing, the Court asked "whether consideration of validity in an infringement action may be precluded by either (a) a prior BPAI interference decision that is subject to judicial review or (b) a contemporaneous decision of a district court in a co-pending Section 146 action." (Jan. 30, 2012 Order).

a particular issue has reached such a stage that a court sees no really good reason for permitting it to be litigated again." *O'Reilly v. Malon*, 747 F.2d 820, 823 (1st Cir. 1984). Here, the BPAI decision remains subject to reconsideration in the pending Section 146 action.

Abbott insists that the BPAI decision is final notwithstanding the pending Section 146 action because that action is merely a form of appeal. Generally, the pendency of an appeal in a prior judicial action does not prevent the decision in that action from having the effect of issue preclusion. *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1378-79 (Fed. Cir. 1999). However, although Section 146 is typically referred to as a means to "appeal" decisions of the BPAI, the statute in fact creates a more complicated form of action—what the Federal Circuit has called a "hybrid of an appeal and a trial *de novo*." *Winner*, 202 F.3d at 1345 (quoting *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 592 (Fed. Cir. 1997)).[18] Indeed, where live testimony (which cannot be presented before the BPAI) is offered in a Section 146 action, the entire proceeding becomes a trial *de novo*, in which the district court "treat[s] the record before the Board when offered by a party 'as if it was originally taken and produced' in the district court." *Winner*, 202 F.3d at 1347 (quoting 35 U.S.C. § 146). Because this statutory scheme creates a possibility of a *de novo* trial on the validity issues that were first decided by the BPAI, the decision of that administrative body cannot be a "binding final judgment" with preclusive effect in

[18] This unique form of review is contemplated by Section 146 itself, which provides:

> In [Section 146] suits the record in the Patent and Trademark Office shall be admitted on motion of either party . . . without prejudice to the right of the parties to take further testimony. The testimony and exhibits of the record in the Patent and Trademark Office when admitted shall have the same effect as if originally taken and produced in the suit.

35 U.S.C. § 146.

this infringement action.[19]

This conclusion is consistent with cases in which courts have held that certain BPAI decisions had preclusive effect. Those cases are limited to situations where the party that lost before the agency declines to seek judicial review of the interference decision within the period for review prescribed by Section 146 and its implementing regulations. *See* 35 U.S.C. § 146; 37 C.F.R. § 1.304 (establishing two-month limitations period for filing Section 146 action for review of interference decision). Once the period for review has elapsed, courts have deemed the BPAI decision to have "the same finality as the judgment of . . . the courts would have had if one of them had reviewed it." *Coakwell v. United States*, 292 F.2d 918, 920 (Ct. Cl. 1961); *see also William T. Burnett & Co. v. General Tire & Rubber Co.*, 203 U.S.P.Q. 801, 802 (4th Cir. 1979) ("Resolution of this controversy rests upon the determination by Burnett not to pursue its various contentions in a suit to review the decision in the Interference, as permitted by statute."); *see also Meritor Transmission Corp. v. Eaton Corp.*, 2006 WL 3951711, at *7 (W.D.N.C. Sept. 26, 2006) ("Defendant chose not to appeal the Board's judgment and, therefore, the Board's judgment became final [for purposes of issue preclusion]"). These cases thus support the proposition that a BPAI decision becomes a "final judgment" only after it has been reviewed or after the passing of the limitations period bars the losing party from seeking review in court.

However, this case comes to the Court in a different posture. Not only did Centocor file a timely Section 146 action after it lost in the PTO, but that action is currently pending before this

[19] In other contexts, decisions that are subject to *de novo* review have not been considered final for purposes of issue preclusion. *See Lawson v. FMR L.L.C.*, 724 F. Supp. 2d 141, 151-52 (D. Mass. 2010), *rev'd on other grounds, Lawson v. FMR L.L.C.*, 2012 WL 335647, 18 (1st Cir. Feb. 3, 2012); *Nixon v. Richey*, 513 F.2d 430, 438 (D.C. Cir. 1975) ("The federal rule is that pendency of an appeal does not suspend the operation of a final judgment for purposes of collateral estoppel, except where appellate review constitutes a trial *de novo*.") (citing *Huron Holding Corp. v. Lincoln Mine Operating Co.*, 312 U.S. 183, 188-89 (1941).

Court. Only one case brought to the Court's attention directly addresses issue preclusion in this context. In *Streck v. Research & Diagnostic Sys.*, 2010 WL 519817 (D. Neb. Feb. 5, 2010), Streck brought an infringement action against R & D during the pendency of a PTO interference proceeding to which they were both parties. Five days after the jury returned a verdict in favor of Streck, the BPAI ruled in favor of R & D on the issue of priority and thereby invalidated Streck's patent. Streck then brought a timely Section 146 action for review of the interference decision in the same district court that had heard the infringement action. R & D filed a motion to vacate the judgment in the infringement action and stay that proceeding pending resolution of the Section 146 action, "based on its contention that the Board's priority decision operates to collaterally estop Streck from enforcing the court's judgment." *Id.* at *1. The district court denied R & D's motion, reasoning that, "Streck has challenged the decision of the Board under 35 U.S.C. § 146 in an action presently pending in this court . . . . Accordingly, the decision of the Board is not a final decision and cannot be accorded collateral estoppel effect." *Id.* It subsequently reversed the BPAI and found the patent valid, as the jury had. *Streck, Inc. v. Research & Diagnostic Sys., Inc.*, 744 F. Supp. 2d 970, 986 (D. Neb. 2010). This Court agrees with the court in *Streck* that a BPAI decision is not a "final judgment" for purposes of issue preclusion during the pendency of a Section 146 action appealing that decision.

Here, Centocor has asserted its statutory right to judicial review of the interference decision, and that action is concurrently pending with this action. The availability of plenary review of the BPAI decision under Section 146 means, in the language of one early patent decision, that the administrative decision has not yet been "fortified by judicial decree or judgment or acquiescence." *Minneapolis Harvester Works v. McCormick Harvesting-Mach. Co.*, 28 F.

565, 566 (C.C.D. Minn. 1886) (denying motion for preliminary injunction in infringement action where injunction would be based on interference decision regarding validity, on the grounds that the interference decision alone was "far from *res adjudicata*"). Thus, because the BPAI decision is not yet a "final judgment," it does not preclude Centocor from raising invalidity defenses in this infringement action. *See Ramallo Bros,* 490 F.3d at 90.

2. Section 146 Action

Abbott argues that because the Section 146 action would have preclusive effect if it were concluded before the infringement action began, the Court has discretion to decide validity first in the Section 146 action, with the effect of precluding the issue in the infringement trial. For the following reasons, the Court will not exercise its discretion in this way because doing so would inappropriately impair Centocor's right to have this issue decided by a jury.

The Seventh Amendment provides that "[i]n Suits at common law . . . the right of trial by jury shall be preserved, and no fact tried by a jury, shall be otherwise reexamined . . . ." Analysis of whether there is a Seventh Amendment right to jury trial of a given claim generally hinges on whether the claim was considered one "at common law" or one "at equity" at the time of the adoption of the amendment. *See, e.g., Feltner v. Columbia Pictures Television, Inc.*, 523 U.S. 340, 348 (1998). Here, the infringement action constitutes a legal action to which the right to a jury attaches, while the Section 146 action is an equitable proceeding ordinarily subject to trial by the court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 377 (1996) ("[I]nfringement cases . . . must be tried to a jury."); *General Instrument*, 995 F.2d at 214 ("[R]eview of an interference proceeding under Section 146 is an equitable remedy of long standing."). It therefore seems clear that, had the Section 146 action been concluded before Abbott filed this lawsuit,

validity determinations in that prior equitable proceeding would have preclusive effect here. If the Court invalidated the patent in the Section 146 action, the former patentee would have no right to instigate a subsequent infringement action at all. *See* 35 U.S.C. § 281. Alternatively, if the Court found that Centocor did not prove invalidity by a preponderance of the evidence, Centocor would be unable to prove invalidity in the infringement action under the clear-and-convincing standard because the finding in the earlier action would logically preclude its success under the higher standard in the later one.[20] Thus, the determination of the Section 146 action by the Court before the infringement action is tried by a jury would, in effect, curtail Centocor's right to have certain factual issues decided by a jury.

In *Beacon Theatres, Inc. v. Westover*, 359 U.S. 500 (1959), the Supreme Court addressed the applicability of the Seventh Amendment right to a jury trial in circumstances where a court is simultaneously confronted with both equitable and legal claims that share common factual issues. In that case, the defendant answered the plaintiff's equitable claim for injunctive relief with a legal

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[20] The Federal Circuit recently addressed the significance of a prior Section 146 action and a later infringement decision in *Streck, Inc. v. Research & Diagnostic Sys., Inc.*, 665 F.3d 1269 (Fed. Cir. 2012) ("*Streck II*"). In that case, the decisions of a district court in concurrent infringement and Section 146 actions between the same parties were both appealed by R & D, which had lost in both proceedings. The Federal Circuit decided the Section 146 appeal first, and found that R & D had failed to prove invalidity by a preponderance of the evidence. *Streck, Inc. v. Research & Diagnostic Sys., Inc.*, 659 F.3d 1186, 1196 (Fed. Cir. 2011) ("*Streck I*").

In its subsequent decision on the infringement appeal, the court found this issue precluded from its consideration:

> [I]n the § 146 action, R & D had to establish priority by a preponderance of the evidence whereas in this appeal, R & D had to show its priority defense by clear and convincing evidence. [Therefore], our decision in [*Streck I*] that R & D failed to establish priority by a preponderance of the evidence necessarily means that R & D could not meet the clear and convincing burden required in this case . . . . In addition, as Streck argues, because the § 146 appeal involved the same parties, the same evidence, and the same priority issue presented in this appeal, R & D is barred by the doctrine of collateral estoppel from challenging this court's priority determination.

Streck II., 665 F.3d at 1292. *See also Parklane Hosiery Co., Inc. v. Shore*, 439 U.S. 322, 335 (1979) (endorsing the view that "an equitable determination can have collateral-estoppel effect in a subsequent legal action").

counterclaim for damages. The district court severed the two sets of claims for trial pursuant to Fed. R. Civ. P. 42(b) and conducted a bench trial on the equitable claim first. It was apparently understood that this arrangement "might, through collateral estoppel, prevent a full jury trial" on the legal counterclaim. *Id.* at 505. The court then granted summary judgment with respect to the legal claims, reasoning that its factual determinations in the bench trial would preclude a jury trial on the same issues. *Id.* at 503-04. The Supreme Court held that "the use of discretion by the trial court under Rule 42(b) to deprive Beacon of a full jury trial on its [legal claims] . . . cannot be justified." *Id.* at 508. It reasoned that "only under the most imperative circumstances . . . can the right to a jury trial of legal issues be lost through prior determination of equitable claims." *Id.* at 510-11; *see also Dairy Queen, Inc. v. Wood*, 369 U.S. 469, 479 (1962) (holding that when legal claims involve factual issues that are "common with those upon which [a party's] claim to equitable relief is based, the legal claims involved in the action must be determined prior to any final court determination of [the] equitable claims").

Of course, the equitable and legal claims related to validity that are at issue here do not arise in the same action. Rather, the infringement action and the Section 146 action were filed separately, in different courts, and by different parties (Abbott filed the infringement action, while Centocor filed the Section 146 action). Abbott argues that where equitable and legal claims are not raised within the same action, the decision in *Parklane Hosiery*, 439 U.S. 322 (1979), requires that the final resolution of common factual issues in a bench trial on the equitable claim will preclude their subsequent trial by jury on the legal claim. In *Parklane Hosiery*, a stockholder's class action was brought against a corporation on allegations that the corporation issued a false and misleading proxy statement. 439 U.S. at 325. Before that legal action reached

trial, the Securities and Exchange Commission brought suit against the same corporation based on substantially similar factual allegations. *Id.* Although the two cases were filed in the same district, they were assigned to different judges. *See Shore v. Parklane Hosiery Co., Inc.*, 565 F.2d 815, 816-18 (2d Cir. 1977). A bench trial was held in the SEC suit, and the district court found that the proxy statement was materially false and misleading. *Parklane Hosiery*, 439 U.S. at 325. The plaintiffs in the stockholder action then filed for summary judgment that the corporation was precluded from re-litigating the same issue in that suit. *Id.* On appeal, the Second Circuit held, and the Supreme Court affirmed, that the Seventh Amendment was not violated by the preclusion of issues in the jury trial by the previous determination of those issues in the equitable proceeding. *Id.* at 325, 335. It distinguished *Beacon Theatres* as establishing "no more than a general prudential rule" that "the trial judge has only limited discretion in determining the sequence of trial and 'that discretion . . . must, wherever possible, be exercised to preserve jury trial.'" *Id.* at 334 (quoting *Beacon Theatres*, 359 U.S. at 510).

This case, however, is distinguishable from *Parklane Hosiery*, and the "prudential rule" of *Beacon Theatres* is the guiding principle best suited to its unusual procedural posture. In *Parklane Hosiery*, the legal and equitable suits were each brought by a different plaintiff (the stockholder class and the SEC, respectively). The two actions were heard before separate judges, and so the fact that the equitable action was resolved first was a matter of chance rather than the result of considered judicial discretion. Thus, the holding in *Parklane Hosiery* concerned only whether the Seventh Amendment required a limitation on the finality and preclusive effect of factual findings from a concluded equitable action in an ongoing legal action in another court. Here, by contrast, the consolidation of two suits between Abbott and Centocor operates more like

a single, albeit complex, proceeding. The parties acknowledge that as a procedural matter, it is within this Court's discretion to hold the infringement trial before, after, or concurrently with its determination of the Section 146 appeal. The issue is therefore not whether certain applications of issue preclusion may, under some circumstance, conflict with the Seventh Amendment, but whether constitutional considerations should lead the Court to order the trials in one manner as opposed to another. This matter of case management is precisely the kind of discretionary judgment that, under *Beacon Theatres*, "must, wherever possible, be exercised to preserve jury trial." *Beacon Theatres*, 359 U.S. at 510. Because *Beacon Theatres* precludes the discretionary severance for trial of an equitable claim from a legal claim between the same parties under Fed. R. Civ. P. 42(b), it would be odd if this Court could cut off one party's right to a jury simply by the discretionary manner in which it consolidates and manages these actions under Rule 42(a).

Other courts considering the interplay between equitable and legal claims in patent actions have likewise managed such "mixed" cases so as to preserve the right to have facts determined by a jury. *See Shum v. Intel Corp.*, 499 F.3d 1272, 1279 (Fed. Cir. 2007) (holding that district court erred in holding bench trial on inventorship claim and subsequently granting summary judgment in state-law claims that depended on common factual disputes); *Herman v. William Brooks Shoe Co.*, 1998 WL 832609, at *4 (S.D.N.Y. Dec. 1, 1998) (holding that factual issues common to an inequitable conduct and a validity claim must be tried by a jury). Granted, those cases involved claims that were raised within the same action (that is, in a single complaint or its answer). Abbott emphasizes this point in support of its position that *Beacon Theatres* has no relevance where concurrent but separate actions present a court with both legal and equitable means for resolving common facts. However, the Supreme Court's reliance in *Parklane Hosiery* on a

distinction between claims within one action and those in separate actions reflected not a rigid technical rule but rather a practical recognition that the existence of separate actions usually results in a particular sequence in which the actions are resolved. The Supreme Court's holding that the earlier-decided case precluded re-litigation of the same issues in the later action did not assign any particular significance to the fact that the actions were separate. Rather, its decision was based on the rationale that, once a prior equitable action has concluded, "there is no further factfinding function for the jury to perform, since the common factual issues have been resolved in the previous action." 439 U.S. at 336. But where the two actions are concurrently pending before one court, that principle has no application. Instead, *Beacon Theatres* requires that the factfinder's function should, if reasonably possible, be performed by a jury.

Abbott suggests that allowing the jury to make the first determination with respect to patent validity will have the perverse effect of giving Centocor two opportunities to litigate the same issue. That possibility follows inevitably from the different standards of proof that apply in the two actions. In the infringement trial, Centocor bears the burden of proving invalidity by clear and convincing evidence. 35 U.S.C. § 282; *Microsoft*, 131 S. Ct. at 2242. If it fails to meet that burden, it may nonetheless have the chance, in the Section 146 action, to obtain a reversal of the BPAI decision if it establishes that the patent is invalid by a preponderance of the evidence. *Rexam*, 30 Fed. Appx. at 985. Abbott contends that an arrangement that allows Centocor two bites at the apple in contesting the patents' validity is inefficient and unfair. The problem, however, is that any such inefficiency or unfairness can only be avoided by eliminating or impairing Centocor's right to a jury trial. The arrangement that preserves that right, while not free from imperfection, is most consistent with the tenets of the Seventh Amendment and the

Patent Act's system for adjudicating patent validity.

The invalidity claims will therefore be tried first to a jury. Once that proceeding has concluded, the Court will take up whatever matters remain for resolution in the Section 146 proceeding.[21]

Accordingly, Abbott's motion for summary judgment as to the applicability of issue preclusion to Centocor's validity arguments will be denied.

B. Indefiniteness

Centocor seeks a ruling that certain claims, which it calls the "K_d claims," are invalid for indefiniteness.[22] Abbott has cross-moved for a ruling that the claims are not indefinite.

Section 112 of the Patent Act provides that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, ¶ 2. It follows that, as a condition of validity, each patent claim must be sufficiently definite that "one skilled in the art would understand the bounds of the claim when read in light of the specification." *Exxon Research and Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001). A claim is not indefinite as long as its meaning is "discernible, even though the task [of claim construction] may be formidable and the conclusion may be one over which reasonable persons will disagree." *Id.* at 1375. Rather, a claim is invalid for indefiniteness only if it is "insolubly ambiguous, and no narrowing construction can properly

[21] To the extent that this Court has a factfinding function, it will hear the same evidence as the jury at the same time to avoid unnecessary duplication and expense. If additional testimonial evidence needs to be taken, the Court will hear it outside the presence of the jury. Of course, the factual findings of the jury may, in some circumstances, be binding on this Court, either in whole or in part.

[22] The K_d claims are claims 1-15, 27-28, 50-64, and 70 of the '128 patent and claims 11 and 24 of the '485 patent.

be adopted." *Id.* at 1378.

Claim indefiniteness is an issue of law to be decided by the court. *Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d 1325, 1331 (Fed. Cir. 2010). While "a court may consider or reject certain extrinsic evidence in resolving disputes en route to pronouncing the meaning of claim language, the court is not crediting certain evidence over other evidence or making factual evidentiary findings. Rather, the court is looking to the extrinsic evidence to assist in its construction of the written document." *Exxon Research*, 265 F.3d at 1376 (internal quotations omitted). Because indefiniteness renders a claim invalid, it must be proved by clear and convincing evidence to overcome the presumption of validity. *Halliburton Energy Servs., Inc. v. M-I L.L.C.*, 514 F.3d 1244, 1249 (Fed. Cir. 2008); *see also Exxon Research*, 265 F.3d at 1380 ("[C]lose questions of indefiniteness . . . are properly resolved in favor of the patentee.").

Claim 1 of the '128 patent is representative of the K_d claims. It describes "[a]n isolated human antibody, or antigen-binding portion thereof that binds to human IL-12 and dissociates from human IL-12 with a K_4 of 1×10^{-10}M or less and a k_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance." ('128 col. 385 ll.11-15). The threshold values vary, but all the K_d claims include a limitation consisting of a particular K_d value, "as determined by surface plasmon resonance." The patent specifications indicate that SPR measurements may be taken using a biosensor matrix such as the BIAcore system and name four scientific articles describing the process. ('128 patent col. 28 ll.7-17; '485 patent col. 26 ll. 37-46).

The K_d claims were addressed in the claim construction proceedings. In its May 5 order, this Court adopted the parties' agreed-to constructions of the terms "K_d" and "surface plasmon resonance." Under these constructions, "K_d" referred to "the dissociation constant of a particular

antibody-antigen interaction" and "surface plasmon resonance" referred to "an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix." Although both parties agreed to these meanings, Centocor now argues that, as used in the K_d claims, the terms are "insolubly ambiguous" and that the claims are therefore indefinite.[23]

Specifically, Centocor contends that a person reasonably skilled in the art would not be able to measure the K_d value of an antibody using SPR without additional information and therefore could not know if a particular product infringed the claim. SPR tests are conducted under specific experimental conditions. At least two such conditions, surface density and flow rate, themselves influence the antibody-antigen interaction that is the subject of the SPR measurements. (Pearson Ex. 5, Robinson Rpt. ¶¶ 13, 24). This influence means that SPR assays may yield different K_d values for the same antibody when it is tested using different experimental parameters. (Pearson Ex. 6, Myszka Dep. Tr. at 29-30, 103-104, 125-126). Centocor argues that the K_d claims are indefinite because they do not specify the surface density or flow rate parameters under which the K_d value of a potentially infringing product should be measured.[24]

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[23] The fact that the Court construed a claim term during the *Markman* proceedings does not necessarily defeat an indefiniteness argument made with respect to a claim limitation in its entirety. *See Power-One, Inc. v. Artesyn Tech., Inc.*, 599 F.3d 1343, 1348-51 (Fed. Cir. 2010); *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1371 (Fed. Cir. 2008).

[24] Centocor asserts its indefiniteness argument as an alternative to its argument of non-infringement of the K_d claims. Example 5 of the specifications provides surface capacity and flow rate parameters under which Abbott tested its antibodies. Dr. Robinson reports that, when he tested Stelara using the parameters listed in Example 5, the drug did not exhibit K_d values within the scope of the K_d claims. (Pearson Ex. 7, Robinson Rebuttal Rpt. ¶¶ 34-36). Centocor argues that because Example 5 provides the only specific experimental protocol in the patent, the evidence that Stelara does not infringe as measured under the protocol proves either (1) that Stelara does not infringe or (2) that the claims are indefinite.

The relevance of Example 5 is suspect, as it appears to describe a test of the *capacity* of J695 to bind to IL-12 rather than a measurement of kinetic binding properties. ('128 Patent col. 117 l. 8). In any event, the Court

In response, Abbott argues that a K_d value is an intrinsic property of an antibody-antigen interaction that can be determined definitively by surface plasmon resonance. It argues that a person of reasonable skill in the art at the time of the patent filing would not require the specification of proper experimental protocol in order to understand the bounds of a the K_d claim limitations. Instead, Abbott asserts that one skilled in the field, applying known best practices, would conduct pilot experiments to determine appropriate surface density and flow rate conditions prior to measurement.

Centocor relies on *Honeywell Int'l, Inc. v. International Trade Comm'n*, 341 F.3d 1332 (Fed. Cir. 2003). In *Honeywell*, the Federal Circuit considered the construction of a claim-limitation term that "include[d] a numeric limitation without disclosing which of multiple methods of measuring that number should be used." *Halliburton*, 514 F.3d at 1249 (characterizing *Honeywell*). Three methods of measurement were known and accepted in the art, and each yielded a different measurement than the others. The court held that because the patent did not specify which method to use and because the choice of method would determine whether a product met the numeric limitation, the claim was indefinite. *Honeywell*, 341 F.3d at 1340.[25]

Abbott relies on a set of cases that stand in contrast to *Honeywell*. In *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1367 (Fed. Cir. 2011), the Federal Circuit reversed a ruling

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finds that the K_d claims are sufficiently definite notwithstanding the omission of surface density or flow rate parameters, as explained below. Thus, the observed results when Stelara was tested under the protocol described in Example 5 go to infringement and raise an issue for the jury. *See SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1341 (Fed. Cir. 2005) ("The parties' dispute over the proper testing method is therefore a factual question . . . properly submitted to the jury.").

[25] Centocor also cites *Datamize, L.L.C. v. Plumtree Software, Inc.*, 417 F.3d 1342 (Fed. Cir. 2005), in which the Federal Circuit held a claim invalid where it included the limiting term "aesthetically pleasing." The court explained that because the meaning of the term is "completely dependent on a person's subjective opinion," the limitation was indefinite. *Id.* at 1349.

of indefiniteness where a claim limitation specified properties of a plastic as measured by a particular process, but failed to disclose specific moisture conditions to be used in applying that process. Finding that determining moisture conditions for the particular type of test identified was a "routine concern" in the field, the court held that "[w]ell known industry standards need not be repeated in a patent." Because "the record show[ed] that a person of ordinary skill in the art in this field would follow standard industry guidance for conditioning plastics for [the testing process]," the court held that the claim was sufficiently definite. *Id.* Similarly, in *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 655 F.3d 1364 (Fed. Cir. 2011), the Federal Circuit upheld the validity of a claim that provided for a tobacco-curing process in a "controlled environment" but did not specify quantitative limits for various parameters for that environment, such as humidity and temperature. The court explained that exact numbers were not required because curing conditions varied "for each cure" and "the record repeatedly show[ed] that a person of skill in the art of tobacco curing would possess adequate understanding to manipulate these variables to create a controlled environment." *Id.* at 1374.

These two sets of cases are consistent. *Honeywell* stands for the proposition that when multiple acceptable standards or methods for measuring whether a product meets a claim limitation exist and the choice of method will affect the resulting measurement, the patent must specify the appropriate standard or method. *Wellman* and *Star Scientific* stand for the proposition that, when a claim does specify the method of measurement, its omission of details about how to implement the method will not invalidate the claim if a person of ordinary skill in the art could infer those details from industry standards or professional judgment. The issue here is therefore whether a person of skill in the art would require specification of surface density and

flow-rate parameters to determine whether an antibody-antigen interaction exhibited a particular K_d value.

The record demonstrates that a person of skill in conducting SPR assays could discern the bounds of the K_d limitations. Both Centocor's expert, Dr. Robinson, and Abbott's expert, Dr. Myszka, agree that measurements of rate constants in SPR assays vary with experimental conditions and that experimental protocol can influence results. (Pearson Ex. 5, Robinson Rpt. ¶¶ 13, 24; Oyloe Ex. 37, Myszka Rebuttal Rpt. ¶¶ 48-50). However, Dr. Myszka has explained that "[w]hile Dr. Robinson correctly lists a number of variables that can 'influence' Biacore results . . . , best practices account for and consider these variables and thereby can provide reliable data." (Oyloe Ex. 37, Myszka Rebuttal Rpt. ¶ 51). Thus, he concludes, a "person of ordinary skill would have known to examine pilot data" to achieve a suitable surface density and "to design pilot experiments to determine [the effects of flow rate]" on observed rate constants. (*Id.* ¶¶ 57, 60).

Centocor provides no expert testimony contradicting this explanation.[26] Its own employee, Eilyn Lacy, testified that SPR assays conducted by Centocor itself typically use pilot experiments that allow for the adjustment and optimization of variable experimental conditions for specific antibody-antigen assays. (Oyloe Ex. 45, Lacy Dep. Tr. at 47, 54-55, 82-83). In his

[26] In fact, only one explicit dispute is acknowledged in the expert reports. In his rebuttal report, Dr. Myszka states, "I do not agree with Dr. Robinson's claim that '[f]or example, an antibody may be immobilized by a non[-]covalent interaction with a second antibody on the sensor surface that binds to the constant region of the antibody and orients it so that the antigen binding sites are away from the sensor surface." (Oyloe Ex. 37, Myszka Rebuttal Rpt. ¶ 51; Pearson Ex. 5, Robinson Rpt. ¶ 29). The subject matter of this dispute is merely whether one source of experimental variability exists. Because Abbott acknowledges that experimental variability exists and explains that a person skilled in the art would account for that variability, this dispute does not preclude summary judgment. *See Scott v. Harris*, 550 U.S. 372, 380 (2007) ("[T]he mere existence of some alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment; the requirement is that there be no genuine issue of material fact.") (internal citations omitted).

report, Dr. Robinson asserted only that rate constants (k_{on} and k_{off}) "vary based on properties intrinsic to the proteins and can vary depending on the particular conditions of the solution or the assay." (Pearson Ex. 5, Robinson Rpt ¶ 13). Nothing in his report contradicts Abbott's position that K_d is nonetheless a measurable intrinsic property. The Court thus concludes that, although observed results in SPR assays are affected by surface density, flow rate, and other variables, one skilled in the art could optimize measured results through experimentally determined controls without relying on the patent specification to determine those parameters.

Moreover, handbooks on the use of BIAcore instruments issued by BIAcore itself prior to the '128 patent application establish that appropriate methods for conducting SPR experiments were known at the time of the patent application. (Oyloe Declr. Ex. 38 and 68, BIAapplications Handbooks (dated 1994); Ex. 39, BIAsimulation Software Handbook (dated 1996); Ex. 40,BIAtechnology Handbook (dated 1994); Ex. 41, BIACORE 2000 Instrument Handbook (dated 1998); Ex. 42, BIACORE 3000 Instrument Handbook (dated 1999); Ex. 43, BIAevaluation 3.0 Software Handbook (dated 1997); Ex. 44, BIAcore 1000 Instrument Handbook (dated 1995)). Each of these handbooks contains guidance concerning experimental design and the analytical techniques necessary for measurement of kinetic constants and binding properties. The BIAapplications Handbook, in particular, contains a chapter on how "both kinetic and affinity constants can be derived" through SPR assays. It gives guidance on the appropriate surface density (Ex. 68, BIAapplications Handbook, at 5.3.3) and flow rate (*Id.* at 5.3.6). These documents set forth common practices and standards by which, in 1999, a person of reasonable skill in the field could use SPR assays to measure rate constants without being provided specific surface-density and flow-rate parameters.

Scientific literature from the same period provides further evidence that the state of the art allowed determination of proper experimental conditions. In a July 1999 article (published after Abbott's March 1999 application date but collecting material published in previous years), Dr. Myszka explained techniques for controlling variables, including surface density and flow rate, to improve the accuracy of measurements in antibody-antigen interactions. (Oyloe Declr., Ex. 46). That article further supports Abbott's position that, in March 1999, disclosing surface-density and flow-rate parameters was not necessary to describe with sufficient definiteness a claim limitation consisting of a K_d value to be determined by surface plasmon resonance.

Abbott describes the guidance provided in the BIAcore handbooks and then-existing scientific literature as industry "best practices." Centocor contends that the absence of the phrase "best practices" in those materials indicates that a person of skill in the art would not have known, in 1999, the bound of the K_d claim limitations. Claim definiteness does not hinge on magic words. The record clearly indicates that standards existed in the field for the measurement of antibody-antigen affinity. That is sufficient, regardless whether those standards were actually labeled as "best practices."

Finally, Centocor's position that claims of this nature are indefinite is belied by the fact that similar limitation language appears in many patents covering similar subject matter. Abbott identifies 36 U.S. patents that include claims encompassing antibodies with particular binding characteristics as measured by SPR, none of which list specific experimental parameters for the SPR assays. (Oyloe Ex. 49, Kim Declr. ¶¶ 2-38). Centocor itself is the assignee named on three of these patents (U.S. Patent Nos. 7,935,344; 7,560,112; and 7,491,391). Although not determinative, the fact that terminology similar to that in the K_d claims is prevalent in patents

within the same field suggests that those skilled in the art understand such language as sufficiently definite to describe the bounds of what is claimed.

In sum, although SPR assay results may vary depending on various initial testing parameters, the phrase "as determined by surface plasmon resonance" describes a single identifiable experimental method. Because there is no ambiguity as to the measurement methodology contemplated by the K_d claims, Centocor's reliance on *Honeywell* is misplaced. Claims citing a specific method may omit details concerning how to apply that method if a person skilled in the art would have been able, without further information, to identify whether an invention fell within the scope of the claim. *Wellman*, 642 F.3d at 1367. Here, the record shows that a person skilled in the art at the time of Abbott's patent could discern the bounds of a K_d limitation by SPR assays without being provided with specific surface-density or flow-rate parameters. The claims therefore satisfy the definiteness requirement of 35 U.S.C. § 112.

Accordingly, as to the issue of claim definiteness, Centocor's motion will be denied and Abbott's motion will be granted.

C. Written Description

Centocor seeks summary judgment that certain claims in the '128 and the '485 patents are invalid for lack of adequate written description.

The written-description requirement is contained in Section 112 of the Patent Act. The first paragraph of that section provides:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112. A patent claim is therefore invalid unless the disclosure in the specification "clearly allow[s] a person of ordinary skill in the art to recognize that the inventor invented what is claimed." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (internal quotation marks omitted). The written description "must convey with reasonable clarity . . . that, as of the filing date sought, [the patentee] was in possession of the invention." *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008) (internal quotation marks omitted).[27] The sufficiency of a patent's written description is ordinarily a question of fact, but "[a] patent also can be held invalid [as a matter of law] for failure to meet the written description requirement based solely on the face of the patent specification." *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1347 (Fed. Cir. 2011). As with other invalidity defenses, a patentee's failure to comply with the written description requirement must be proved by clear and convincing evidence. *Ariad*, 599 F.3d at 1354.

1. <u>All Asserted Claims</u>

Centocor argues that all claims asserted against it are invalid for failure to satisfy the written-description requirement.[28] The challenged claims are functionally-defined genus claims; that is, each claim defines a family of antibodies based on their ability to bind to and neutralize IL-12 within specific ranges of K_d, k_{off}, and IC_{50} values. Centocor asserts that the patents' disclosure

[27] PTO guidelines state that the written description requirement of 35 U.S.C. § 112 can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). The Federal Circuit adopted this standard in *Enzo Biochem*, 323 F.3d at 964.

[28] These claims include claims 1-2, 4-8, 11-13, 27-30, 32, 38, 50-55, 58, 61, 64, and 70 of the '128 patent and claims 1-4, 6-11, 15-19, and 24-26 of the '485 patent.

of a limited number of representative examples of antibodies within each family is an insufficient written description to support these genus claims.

The Federal Circuit has stated that written-description problems are "especially acute with genus claims that use functional language" because such claims run the risk of "simply claim[ing] a desired result . . . without describing species that achieve that result." *Ariad*, 598 F.3d at 1349. For this kind of claim, the specification must therefore disclose either a "representative number of species falling within the scope of the genus or structural features common to the members of the genus," or the written-description requirement is not met. *Id.* at 1350. Abbott concedes that its patents do not disclose common structural features for the genuses it claims. The sole issue is therefore whether the patents disclose species that constitute a representative set within each genus claim.

There are no "bright-line rules" governing the number of representative species required to support a genus claim, because "this number necessarily changes with each invention, and it changes with progress in a field." *Id.* at 1351. In the biological arts, a patent "cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated." *Noelle v. Lederman*, 355 F.3d 1343, 1350 (Fed. Cir. 2004). Even in an "unpredictable art," however, "every species in a genus need not be described in order that a genus meet the written description requirement." *Eli Lilly*, 119 F.3d at 1568 (citing *In re Angstadt*, 537 F.2d 498, 502-03 (C.C.P.A. 1976) (noting that requiring disclosure of every species within a genus claim would require a prohibitive amount of experimental work of the patentee)).

A patent's failure to comply with the written-description requirement may generally be

determined as a matter of law, *G.D. Searle & Co., Inc.*, 358 F.3d 916, 927 (Fed. Cir. 2004). However, summary judgment is not well-suited to the fact-intensive inquiry necessary to determine how many species are needed to represent a particular genus. *See Capon v. Eshhar*, 418 F.3d 1349, 1360 (Fed. Cir. 2005) (noting that the distinction between "generic inventions that are adequately supported, those that are merely a 'wish' or 'plan' . . . , and those in between" is dependent on the "facts of the specific case").

Thus, courts have not found that disclosure of a particular number of species was insufficient to support a genus claim as a matter of law except in limited circumstances. Some have held that a written description was invalid as a matter of law where the patent failed to disclose a single species of the claimed genus. *E.g.*, *Centocor*, 636 F.3d at 1350-51 ("[W]hile the patent broadly claims a class of antibodies that contain human variable regions, the specification does not describe a single antibody that satisfies the claim limitation.").[29] Others have found disclosure of a single species insufficient to describe certain genus claims. *In re Alonso*, 545 F.3d 1015, 1021 (Fed. Cir. 2008) (affirming finding of invalidity by BPAI where "the one compound disclosed . . . cannot be said to be representative of a densely populated genus."); *Eli Lilly*, 119 F.3d at 1567-68 ("[A] description of rat insulin cDNA is not a description of the broad classes of vertebrate or mammalian insulin cDNA."). However, disclosure of even a single representative embodiment may, in some circumstances, be sufficient to describe a functionally-defined genus.

[29] For other examples of decisions invalidating patents for failure to disclose any representative species, see *Ariad*, 598 F.3d at 1358 (patent disclosed no confirmed species, but "at best" disclosed certain molecules "and hypothesizes with no accompanying description" that they could be used in the claimed process); *G.D. Searle*, 358 F.3d at 927 (patent "[did] not disclose any compounds that can be used in its claimed methods"); *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993) (holding that "[a] bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description" adequate to support a claim to a particular class of DNA absent description of at least one example of DNA within that class).

See Invitrogen Corp. v. Clontech Labs., Inc., 429 F.3d 1052, 1073 (Fed. Cir. 2005) (affirming summary judgment that the written description requirement had been met where the disclosure "recite[d] both the DNA and amino-acid sequences of a representative embodiment"). Here, where the patents disclose 50 antibodies within the scope of the asserted genus claims, summary judgment of invalidity on grounds of the number of representative species alone is unwarranted.[30] *Cf. Angstadt*, 537 F.2d at 503 (upholding BPAI determination that written-description requirement was met by disclosure of forty species within the genus).[31]

Centocor contends that the disclosed species do not adequately reflect the variability of the claimed genuses, regardless of their number. Specifically, it asserts that the antibodies disclosed represent a narrower class than the claimed genuses because the genuses encompass a varied range of amino-acid sequences, but the disclosed antibodies are all derived from a single "lineage" originating with the Joe 9 antibody.[32] The antibodies within this lineage have a high degree of sequence homology, meaning that much of their amino-acid sequencing is the same. The amino-acid sequences of Stelara, by contrast, are substantially different from those of the Joe 9 lineage.[33] If Stelara falls within the claimed genus, Centocor concludes, the genus is too broad

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[30] The specifications disclose 50 antibodies within the scope of the patents' broadest claim. Other claims encompass narrower genuses, and fewer of disclosed embodiments meet the limitations of those claims.

[31] In *Angstadt*, the court's holding concerned the enablement requirement of 35 U.S.C. § 112, not the written-description requirement. 537 F.2d at 500. However, the Federal Circuit has subsequently explained that the option of meeting the written-description requirement for a genus claim by disclosing a representative number of species is "analogous to enablement of a genus under § 112, ¶ 1, by showing the enablement of a representative number of species within the genus." *Eli Lilly*, 119 F.3d at 1569.

[32] The Joe 9 antibody was found by screening a phage-display library for antibodies that bind to IL-12. (Pearson Ex. 17, Siegel Opening Rpt. ¶ 54). The inventors then generated a series of new antibodies from Joe 9 by introducing point mutations and testing those antibodies for their ability to bind to IL-12. (*Id.*)

[33] For example, Centocor asserts that 90% of amino acids in all antibodies in the Joe 9 lineage are the same. ('128 Patent fig. 1A-1D). By contrast, J695, one of the disclosed antibodies, shares only 50% sequence

to be adequately represented by antibodies of the Joe 9 lineage alone.

It is true that a highly variable genus requires a greater variety of disclosed species to meet the written-description requirement. *Carnegie Mellon*, 541 F.3d at 1124 ("[W]hen there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus"). However, summary judgment on this issue is unwarranted because the parties' experts dispute the significance of the differences in amino-acid sequences on which Centocor relies.

First, Abbott offers expert testimony that the Joe 9 lineage itself contains a substantially varied set of sequences. Although the disclosed antibodies were derived from a common source (Joe 9), those experts assert that the process of random mutation undergone by the antibodies was designed to "mine the full variability" of human IL-12 antibodies, such that it is misleading to characterize the resulting antibodies as a "family" of closely related antibodies. (Oyloe Ex. 78, Marks Rebuttal Rpt., ¶¶ 212, 385, 391-94; Oyloe Ex. 92, Wilson Rpt. ¶¶ 66-74). Assessment of this factual question of the variability of the disclosed embodiments is not appropriate on summary judgment.

Second, Abbott's experts dispute whether sequence homology is a valid indicator of genus variability. Dr. Wilson asserts that a comparison of the amino-acid sequences of different antibodies "reveals little about how similar those antibodies are." (Oyloe Ex. 92, Wilson Rpt. ¶ 45; Oyloe Ex. 78, Marks Rebuttal Rpt. ¶¶ 375-81). While the structural diversity of antibodies

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identity with Stelara. (Pearson Ex. 41, Eck Opening Rpt. ¶ 29). Moreover, Centocor states that the disclosed antibodies all contain heavy protein chains of a single family of heavy chains (out of seven families) and one family (of two) of light chains, while Stelara contains protein chains from other families. (Pearson Ex. 17, Siegel Rpt. ¶¶ 62, 302, 333; '128 Patent col. 41 ll. 1-67, col. 42 ll. 1-13). Finally, Centocor states that Stelara binds to an epitope on IL-12 that is entirely separate from the one to which J695 binds. (Pearson Ex. 41, Eck Rpt. ¶¶ 35-38).

capable of binding to IL-12 may be a factor in determining whether the patents include a representative set of species within their genus claims, the finder of fact, not this Court, must assess the conflicting testimony on this point.

In conclusion, because there are material factual disputes relevant to the adequacy of the written description in the patents for their claims to functionally-defined genuses, summary judgment will be denied as to that issue.

2. p19/p40 Claims

Centocor also asserts that the '485 patent contains a written description that is insufficient to support its "p19 claims"—claims that encompass antibodies that bind to the p40 subunit of both IL-12 and IL-23.[34]

The patent makes one reference to the p19/p40 (IL-23) antigen, in the third example in the specification:

> I. Binding to a Novel IL-12 Molecule
>
> An alternative IL-12 heterodimer has been described, in which the p35 subunit is replaced by a novel p19 molecule. P19 was identified using 3D homology searching for IL-6/IL-12 family members, and is synthesized by activated dendritic cells. P19 binds to p40 to form a p19/p40 dimer, which has IL-12-like activity, but is not as potent as the p35/p40 heterodimer in IFNγ production. Antibodies which recognize p40 alone, but preferably in the context of a p70 molecule (e.g., J695 and Y61, see Example 3H) are expected to also neutralize both the p35/p40 molecules and the p19/p40 molecules.

('485 Patent, col. 111, ll. 30-41). The patent also lists a November 2000 scientific article entitled "Novel p19 protein engages IL-12 p40 to form a cytokine, IL-23, with biological

[34] The p19 claims are claims 1-3, 6-11, 15, 18-19, and 24-26 of the '485 patent. Designating them "p19 claims" is misleading, because the patent does not claim antibodies that bind to the p19 subunit of IL-23, but instead antibodies that bind to the p40 subunit that occurs in both IL-12 (the other subunit of which has a weight of p35) and IL-23 (the other subunit of which has a weight of p19).

activities similar as well as distinct from IL-12." ('485 Patent, at 1).

The patent examiner considered the adequacy of the written description for the p19 claims when Abbott added them to its 10/884,830 application in an amendment dated January 7, 2007. (Pearson Ex. 25, 2007 Amendment). The examiner initially construed the p19 claims broadly to encompass "a genus comprising all possible polypeptides with a molecular weight of 19 kDa." (Pearson Ex. 27, 2007 Office Action, at 4). Because the specification "provide[d] a description of only one possible p19 subunit," he rejected the claims. (*Id.* at 4-5).

Abbott filed a response to the examiner's rejection in which it clarified that its intention was "to encompass only the p19 subunit of IL-23, and not any other protein with a molecular weight of 19 kDa." (Oyloe Ex. 95, Response to Office Action, at 9). In support of that interpretation of the claims, Abbott argued that a person of ordinary skill in the art would find that the term "p19 subunit" as used in the claims referred to the p19 subunit of IL-23, based on the teachings of the specification's third example. (*Id.*). Abbott emphasized that the examiner himself had acknowledged that the specification did include a description of that p19 molecule and therefore satisfied the requirements of 35 U.S.C. § 112. (*Id.*). Upon consideration of Abbott's arguments, the examiner canceled the initial rejection and allowed the p19 claims. (Oyloe Ex. 99, Notice of Allowability).[35]

Centocor first contends that the patent's single-paragraph description of the p19/p40

[35] Abbott suggests that Centocor is procedurally barred from challenging the p19 claims because it has not introduced new evidence that was not before the examiner when he considered the same issue, citing *Microsoft*, 131 S.Ct. at 2251 ("[T]he jury may be instructed to evaluate whether the evidence before it is materially new, and if so, to consider that fact when determining whether an invalidity defense has been proved by clear and convincing evidence."). That case, however, held only that "new evidence supporting an invalidity defense may 'carry more weight' in an infringement action than evidence previously considered by the PTO" in evaluating whether a party challenging validity has rebutted the presumption of validity by clear and convincing evidence. *Id.* It did not generally prohibit raising validity issues without offering new evidence.

heterodimer is insufficient as a matter of law because it names the antigen by the molecular weight of its subunits instead of by its protein structure.[36] The '485 patent does not claim the IL-12 or IL-23 antigens themselves—it claims only antibodies to them—and therefore structural descriptions of those molecules is not necessary. *See Eli Lilly*, 119 F.3d 1569 (noting that a genus claim may be described by recitation of the coding sequence of a representative number of species within the genus alone). The question is whether a person skilled in the art at the time of filing would have understood from the patent specification that Abbott had in its possession a representative set of antibodies that, based on assays demonstrating an ability to bind to IL-12, it reasonably expected to bind to IL-23. *See Ariad*, 598 F.3d at 1355 ("Prophetic examples are routinely used in the chemical arts, and they certainly can be sufficient to satisfy the written description requirement.").

Claims based on prophetic examples in the specification may be invalid as a matter of law where the disclosure "is not so much an 'example' as it is a mere mention of a desired outcome" with "no descriptive link" between the disclosed invention and the claimed function. *Id.* But that is not the case here. The specification states that "[a]ntibodies which recognize p40 alone, but preferably in the context of a p70 molecule (e.g., J695 and Y61, see Example 3H) are expected to also neutralize both the p35/p40 molecules and the p19/p40 molecules." ('485 patent col. 111 ll. 36-42). That statement describes a feature IL-12 and IL-23 have in common—a specific p40 subunit to which the disclosed antibodies bind—that supports Abbott's assertion that the species

[36] Centocor argues that Abbott's reference to its PTO filing improperly constitutes an "after-stated intention with respect to what their claims cover" that is irrelevant to the patent's validity. (Def.'s Mem. in Supp. # 3). *See Ariad*, 598 F.3d at 1355 (holding that a written description analysis looks to "the filing date sought"). This Court disagrees with that characterization. In both its PTO filing and its brief in this action, Abbott asserted that the patent contained adequate written description at the time of filing.

it discloses as representative IL-12 antibodies are also representative of a class of IL-23 antibodies. A reasonable finder of fact could infer that this reference establishes a "descriptive link" between the disclosure and the p19 claims.

Whether the disclosed antibodies sufficiently describe a genus of IL-23 antibodies may depend on the state of knowledge in the art about IL-23 at the time of filing. However, the state of the art is a factual issue disputed by the parties. Abbott offers evidence that identification of the p40/p19 heterodimer (which would later be named IL-23) was made public at a scientific conference no later than March 4, 2000, before the patent's filing date of March 24, 2000.[37] (Oyloe Ex. 124, Tracey Rpt.). This factual dispute regarding the state of the art alone precludes summary judgment.

The parties also dispute whether the disclosed antibodies adequately represent the genuses claimed by the p19 claims. Centocor cites two cases for the proposition that Abbott's failure to describe the protein structure of the p19 subunit renders its written description insufficient. In *Alonso*, the Federal Circuit affirmed a BPAI decision that a patent lacked written description for a genus of antibodies specific to neurofibrosarcoma where the specification disclosed only one species within that genus. 545 F.3d at 1023. In *Noelle*, the same court affirmed the decision of the BPAI invalidating a patent that "did not provide sufficient support for the claims to the [claimed] human antibody. . . because [it] failed to disclose the structural elements of [the] human . . . antibody or [its] antigen." 355 F.3d at 1349. Both cases are distinguishable procedurally and

[37] Although the application that became the '485 patent was not filed until 2004, as a divisional application it takes the filing date of the parent application. 35 U.S.C. § 120.

on the merits.[39]

In *Alonso*, the court held the patent invalid because it disclosed neither common structural features of the claimed genus nor disclosed a representative number of species within that genus. *See* 545 F.3d at 1021-22 ("The specification teaches nothing about the structure, epitope characterization, binding affinity, specificity, or pharmacological properties common to the large family of antibodies implicated by the method."). In its analysis, the court observed that the patent at issue did "not characterize the antigens to which the [claimed] monoclonal antibodies must bind; it discloses only the molecular weight of the one antigen identified." *Id.* at 1023. This statement may mean that Abbott cannot support a genus claim solely by identifying IL-23 by reference to a subunit with a particular weight. But the '485 patent does more than that; it indicates that IL-23 shares the well-characterized p40 subunit of IL-12, and it refers to scientific literature describing the functions of IL-23. ('485 patent, at 1, col. 111, ll. 30-41). Moreover, the patent in *Alonso* disclosed only a single antibody, which the court held to be "insufficiently representative to provide adequate written descriptive support for the genus." *Id.* at 1018. Here, by contrast, Abbott has disclosed numerous species within the scope of its genus claims.[40] Whether those species are sufficiently representative is a question for the jury.

In *Noelle*, the determination of invalidity was premised on the patent's failure to disclose the structure of either an antibody within the claimed genus or its target antigen. 355 F.3d at

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[39] Procedurally, both cases affirmed BPAI decisions of invalidity. A decision of the BPAI may be upheld if supported by substantial evidence. Here, by contrast, Centocor's motion may be granted only if the Court finds that Abbott establishes no genuine dispute of material fact that, if resolved in its favor, would support a jury verdict that accords with the BPAI decision.

[40] Dr. Marks identifies the antibody species that Abbott asserts fall within each p19 claim. (Oyloe Ex. 78, Marks Rebuttal Rpt. ¶¶ 409-10, 418-19).

1349. Abbott, by contrast, offers evidence that the patent characterizes the claimed genus of antibodies through a representative set of species and that the target antigen, the p40 subunit of IL-23, was known in the art at the time of filing. That is sufficient to create a genuine dispute of fact.

In conclusion, summary judgment will be denied as to whether the written-description requirement was met for the p19/p40 claims because the record establishes relevant factual disputes regarding both the state of the art at the effective filing date and the sufficiency of the disclosed antibodies in representing the claimed genuses.

D. Prior Art

A patent is invalid if it is anticipated by, or is obvious in light of, prior art as defined by Section 102. 35 U.S.C. §§ 102 and 103. As relevant here, that section provides:

> A person shall be entitled to a patent unless—
>
> . . .
>
> (f) he did not himself invent the subject matter sought to be patented, or
>
> . . .
>
> (g)(2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. § 102. Prior invention under Section 102(g)(2) occurs when another inventive entity was "the first party to reduce an invention to practice [or] to conceive the invention and [to exercise] reasonable diligence in later reducing that invention to practice." *Mahurkar v. C.R.*

Bard, Inc., 79 F.3d 1572, 1577 (Fed. Cir. 1996).

If any single prior-art reference contains each limitation of an asserted patent claim, that claim is invalid by anticipation. *See Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1335 (Fed. Cir. 2002). Section 103 provides that prior art, even if not identical to the asserted claim, may render that claim invalid for obviousness, subject to certain exceptions. *See Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1445 (Fed. Cir. 1984). However, a "party asserting invalidity under Section 102(g) must prove facts by clear and convincing evidence establishing a prior invention that was not abandoned, suppressed, or concealed." *Apotex USA, Inc. v. Merck & Co., Inc.*, 254 F.3d 1031, 1036 (Fed. Cir. 2001).

Priority, conception, and reduction to practice are questions of law that are based on subsidiary factual findings. *Cooper v. Goldfarb*, 154 F.3d 1321, 1327 (Fed. Cir. 1998). Where the underlying facts are undisputed, however, prior art issues are amenable to summary judgment. *See Bruckelmyer v. Ground Heaters, Inc.*, 445 F.3d 1374, 1377 (Fed. Cir. 2006).

1. Joe Antibodies

Centocor seeks a ruling that the Joe antibodies are prior art to the patented subject-matter under Section 102(g)(2). Abbott has cross-moved for a ruling that the Joe antibodies are not prior art under either Section 102(f) or 102(g)(2).

As explained previously, scientists working on Abbott's IL-12 project discovered the antibodies known as Joe 7, 9, and 10 in late 1995 and early 1996 by screening a phage-display library for human antibodies that bind to IL-12. These antibodies were subsequently used to develop antibodies for IL-12 with desirable affinity and neutralizing properties.

The parties agree that three Abbott employees—Drs. Salfeld, Tracey, and

Banerjee—came up with the idea of developing a human, neutralizing antibody to IL-12 during a meeting held on July 13, 1993. (Pearson Ex. 31, Abbott Interference Mot. 7, at 5). Centocor argues that this meeting constituted the moment when the Joe antibodies were conceived, and therefore invented for purposes of determining priority.[41] At the time of the June 1993 meeting, Abbott had not yet entered into the collaborative research agreements by which Abbott, CAT, and GI scientists would eventually reduce to practice the Joe antibodies and other IL-12 antibodies that are disclosed in the patents. Centocor contends that because the 1993 meeting pre-dated those research agreements, the three scientists who attended it constituted, at that time, an inventive entity separate from the larger group of inventors named on the patent. Centocor argues that the conception of the Joe antibodies at that meeting was therefore a prior invention by "another inventor" within the meaning of102(g)(2), and that those antibodies are therefore prior art to the patented material. That argument is incorrect for two reasons.

First, the 1993 brainstorming meeting did not constitute the conception of the Joe antibodies. At most, it was the conception of a generic idea of a group of human antibodies to IL-12 that would have pharmaceutical uses. Conception, for purposes of dating an invention, requires a "definite and permanent idea of an operative invention," such that "one of ordinary skill

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[41] Centocor cites several cases for the proposition that invention under Section 102(g)(2) dates to the time of conception: *Loral Fairchild Corp. v. Matsushita Elec. Indus.*, 266 F.3d 1358, 1365 (Fed. Cir. 2001) (Newman, J., concurring); *Pfaff v. Wells Elec., Inc.*, 525 U.S. 55, 60 (1998); *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1227-28 (Fed. Cir. 1994). These cases do articulate the principle that a prior-art reference is dated to the time of conception as long as the inventor exercises diligence in reducing that conception to practice. *Loral Fairchild*, 266 F.3d at 1366 (holding that the date on which an invention is "made" for purposes of priority under 102(g)(2) is the earlier of either "a reduction to practice, or conception of the invention plus diligence to actual or constructive reduction to practice." As explained below, however, under these principles the 1993 meeting marks, at most, the date of a generic invention, not that of the specific Joe antibodies.

It is also notable that Centocor's argument that the Joe antibodies were invented in 1993 is contradicted by the report of Mr. Murphy, which asserts that invention of the antibodies for purposes of 103(g)(2) occurred when they were reduced to practice in 1995 and 1996. (Oyloe Ex. 50, Murphy Rpt. ¶ 103, 105-06).

in the art could [reduce the invention to practice] without unduly extensive research or experimentation." *Sewall v. Walters*, 21 F.3d 411, 415 (Fed. Cir. 1994); *see also Singh v. Brake*, 317 F.3d 1334, 1340 (Fed. Cir. 2003) ("A conception must encompass all limitations of the claimed invention."). When a generic concept requires further research or experimentation before it can be reduced to specific embodiments, it is the conception only of a genus—not of any species within that genus. *Ganguly v. Sunagawa*, 5 U.S.P.Q. 2d 1970, 1972 (B.P.A.I. 1987) ("[C]onception of a genus is not conception of a species.").

Conception of chemical compounds, including biological compounds such as antibody proteins, does not occur until the inventor "has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it." *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991).[42] The mere realization that a substance with a useful "biological property" may exist is not a conception of that substance, because "an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." *Id.*

Here, it is clear that the 1993 meeting merely marked the identification, by Abbott scientists, of the ability to bind to and neutralize IL-12 as a desirable biological property likely possessed by an as-of-then unknown class of antibodies. A July 30, 1993 memorandum

[42] Centocor's own expert, Mr. Murphy, acknowledges that biological inventions, such as antibodies with particular biological properties, may fall within this category of inventions and, further, suggests that antibodies may incapable of being invented under this standard until they are actually reduced to practice. He notes that with some chemical inventions, "the inventor cannot conceive of the structure of a molecule that will have a certain biological activity (such as a protein, enzyme, antibody, DNA, etc.) . . . until the new molecule is actually made, and then tested to determine whether i[t] possesses the intended biological activity." (Oyloe Ex. 50, Murphy Rpt. ¶ 54).

memorializing the July 16 brainstorming meeting describes IL-12 and lists it among several "proposed additional targets for CAT collaboration." (Pearson Ex. 14, July 30 Memo., at ABT-IL12-00324514-15). It explains the understood biological functions of IL-12 and outlines why anti-IL-12 therapy might have medical uses. (*Id.*). There is no indication in the memorandum that the three scientists (or anyone else) had conceived of the structure of any particular IL-12 antibody. (*Id.*).

In sum, the evidence relied on by Centocor to prove conception of the Joe antibodies establishes that, as of July 1993, Drs. Salfeld, Tracey, and Banerjee had not conceived of any specific antibody to IL-12; they had simply announced human antibodies to IL-12 as a subject for further research. Such a "wish to know" does not establish conception. *Amgen*, 927 F.2d at 1206. Thus, the record establishes what common sense dictates: that the identification of a research priority (in 1993) by one subset of the named inventors does not render subsequent products of that research (discovered in 1995 and 1996) prior art to the final invention.[43]

A second independent reason that the Joe antibodies are not "prior art" to the patents is that those antibodies were the work of joint inventors, not "another inventor." Centocor's argument to the contrary rests on the fact that the term "another," as used in the statute, means "any inventive entity other than the inventor," and that two inventive entities are separate as long as "not all inventors are the same." *See* Section by Section Analysis: Patent Law Amendments of 1984 (Oct. 1, 1984), *reprinted in* 1984 U.S.C.C.A.N. 5827, 5834 (Oct. 1, 1984); Manual of

[43] Centocor suggests that a dispute as to the date of conception is created by Abbott's statement before the BPAI that "on about July 16, 1993, and by no later than July 30, 1993, Abbott's conception of the subject matter of Count 1 was complete . . . . All that was necessary at this point was to make the antibody, an event that occurred no later than September 19, 1995." (Pearson Ex. 31, Abbott Interference Motion 7, at 4). Centocor must do more, however, than point to the parties' former litigating positions to establish its preferred priority date by clear and convincing evidence.

Patent Examining Procedure § 2136.04 (8th ed., July 2010 rev.) ("The fact that [the groups] have one or more inventors in common is immaterial."). Thus, it is possible that where a subset of a patent's named inventors independently developed one invention before the larger group invented the patented invention, the older work will be prior art against the newer. Centocor argues that because Drs. Salfeld, Tracey, and Banerjee invented the Joe antibodies before Abbott entered into research agreements with scientists at CAT and GI, those three Abbott scientists constituted a separate "inventive entity" from the larger entity named in the patent.

That position is consistent with 35 U.S.C. § 116, which permits inventors who work together to file jointly for a single patent. In 1984, that section was amended by the addition of a sentence, which provides:

> Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent.

35 U.S.C. § 116, ¶ 1; Pub.L. 98-622, Title I, § 104(a), 98 Stat. 3384 (Nov. 8, 1984). The broad reach of joint inventorship under Section 116 suggests that even if the Joe antibodies were invented at the 1993 meeting, as Centocor contends, that work would not be prior art to the patents, because the scientists at the meeting were joint inventors with the other scientists named in the patents.

Centocor nonetheless argues that Drs. Salfeld, Tracey, and Banerjee cannot be joint inventors because they constitute a separate inventive entity under the holdings of two cases: *In re Land*, 368 F.2d 866 (C.C.P.A. 1966), and *In re Bass*, 474 F.2d 1276 (C.C.P.A 1972). In *Land*, the Court of Customs and Patent Appeals explained that the previous invention of an

individual inventor could be prior art against the joint invention of that individual together with another inventor. 368 F.2d at 881. In *Bass*, the same court held "that the use of the prior invention of another . . . under the circumstances of this case which include the disclosure of such invention in an issued patent, is available as 'prior art' within the meaning of that term in § 103 by virtue of § 102(g)." 474 F.2d at 1286-87.

The holdings of *Land* and *Bass* are in tension with the flexible standard for collaborative research and development contained in Section 116. Moreover, both cases were decided before the 1984 amendments to Section 116 that embraced a broad definition of joint inventorship. Courts have accordingly limited the reach of the doctrine of separate inventive entities as expounded in those cases. Thus, in interpreting Section 119, which governs the priority of U.S. patents for inventions previously patented in other countries, courts have rejected a "hard and fast" rule that the inventive entity for both patents must be identical, citing the "liberalization of the requirements for filing a U.S. application as joint inventors wrought by the 1984 amendment of 35 U.S.C. [§] 116." *Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V. v. Whitehead Inst. for Biomedical Research*, 2011 WL 487828, at *3-4 (D. Mass. Feb. 7, 2011) (quoting *Reitz v. Inoue*, 39 U.S.P.Q.2d 1838, 1840 (B.P.A.I. 1995). Likewise, in interpreting Section 102(e), which bars patents on inventions previously patented by "another," the Federal Circuit has held "[e]ven though an application and a patent have been conceived by different inventive entities, if they share one or more persons as joint inventors, the 35 U.S.C. § 102(e) exclusion for a patent granted to 'another' is not necessarily satisfied." *Applied Materials, Inc. v. Gemini Research Corp.*, 835 F.2d 279, 281 (Fed. Cir. 1987). It would likewise be inconsistent with the structure of the patent act for a joint inventor under Section 116 to be "another inventor"

under Section 102(g)(2) merely because he did not work on the invention during the same period as his collaborators.

Two decisions of regional circuits have narrowed the implications of the holdings of *Land* and *Bass* in the context of analyzing priority of invention.[44] In *General Motors Corp. v. Toyota Motor Co.*, 667 F.2d 504 (6th Cir. 1981), the Sixth Circuit distinguished separate inventorship from circumstances in which inventors within a single corporation undertake separate research efforts toward a common goal. The court explained, "neither *Land* nor *Bass* indicates that the prior inventions were in any way the product of concerted effort within a business entity." *Id.* at 506-07. By contrast, the court held that "[w]here numerous 'inventors' all worked under the aegis of one employer toward a common goal, it is appropriate to define the concept of joint invention broadly. It is not realistic to require in such circumstances that joint inventors work side-by-side, and that each step in the inventive process be taken by all the firm's collaborators." *Id.* The circumstances in this case, in which all named inventors were employees of Abbott or its research partners, are analogous to those in *General Motors*.

Similarly, in *Shields v. Halliburton Co.*, 667 F.2d 1232 (5th Cir. 1982), the Fifth Circuit distinguished *Land* from circumstances in which a sole inventor never seeks a patent on his first invention before contributing it to a later joint invention.[45] The court in *Shields* held that "where

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[44] As regional circuit decisions decided before Congress established the Federal Circuit and before the 1984 amendments, these cases are not binding authority. As analyses of circumstances closely analogous to this case, however, their reasoning is persuasive insofar as it casts light on how joint inventorship may operate when temporal gaps in collaborate inventive processes arguably create separate inventive entities within a single research team.

[45] This inventorship analysis has been cited approvingly, albeit in passing, by both the Federal Circuit and district courts. *See Kimberly-Clark Corp. v. Procter & Gamble Distrib. Co., Inc.*, 973 F.2d 911, 916 (Fed. Cir. 1992); *Ethicon, Inc. v. U.S. Surgical Corp.*, 937 F. Supp. 1015, 1036 (D. Conn. 1996) ("[j]oint invention can exist even if "the major share of the inventive effort is accomplished by one joint inventor working alone prior to the

[one person] does some work, seeks no patent, collaborates with [another], and subsequently they together seek a patent, the joint application declares that their work submitted as a whole is a single invention—the first of its kind." *Compare Bass*, 474 F.2d at 1286-87 ("[W]e . . . hold that the use of the prior invention of another . . . under the circumstances of this case *which include the disclosure of such invention in an issued patent*, is available as "prior art" . . . by virtue of § 102(g).") (emphasis added). To hold otherwise, the Court in *Shields* reasoned, would contravene the purpose of Section 116, "because if the 'first' inventor's initial work for which no patent was sought constitutes an earlier invention as to any subsequent efforts with a collaborator, no valid joint invention would be possible." *Shields*, 667 F.2d at 1235.

Shields suggests that the holding of *Bass* does not compel the conclusion that the alleged invention of the Joe antibodies in 1993 was prior art to the patented inventions. Even if invented in 1993, before the research agreement between Abbott and GI took effect, those antibodies were the unpatented, interim product of what was a single, ongoing, collaborative research effort. It is not necessary to decide now whether an earlier inventor must seek patent protection to become a separate inventive entity. It is enough to hold that, in this case, the initial work of three Abbott scientists was part of a larger collaborative effort that led to the patented inventions. The scientists did not form a separate inventive entity, and their work was not the prior invention of "another inventor" within the meaning of Section 102(g)(2).

As a final point, Centocor contends that if the Joe antibodies were prior art under 102(g)(2), they do not fall within Section 103(c)(1)'s safe harbor for inventions resulting from

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collaboration.") (quoting *Shields*, 667 F.2d at 1235); *Fina Tech., Inc. v. Ewen*, 857 F. Supp. 1151, 1155 (N.D. Tex. 1994).

contractual research agreements. That section provides:

> Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

35 U.S.C. § 103(c)(1). This section was added to Section 103 as one of two amendments apparently enacted to supersede *Bass* and in furtherance of a policy of promoting collaborative research. *See* Pub.L. 98-622, Title I, § 103, 98 Stat. 3384 (Nov. 8, 1984) (adding Section 103(c)(1)); Pub.L. 108-453, § 2, 118 Stat. 3596 (Dec. 10, 2004) (adding Section 103(c)(2)). Centocor argues that the Joe antibodies do not fall within the safe-harbor provisions of Section 103 and therefore Abbott cannot claim the benefits of the partial legislative reversal of *Bass*.[46] The legislative reversal of *Bass* was not limited, however, to the safe-harbor provisions of Section 103(c), particularly where, as here, contemporaneous amendments to Section 116 apply. Because, under Section 116, the Joe antibodies were invented by joint inventors and not by a separate inventive entity, they are not prior art under Section 102(g), and Abbott does not need the benefit of the safe-harbor provisions of Section 103.

Once the legal theories put forward by Centocor have been dismissed, the undisputed facts in the record show that the Joe antibodies are not prior art to the claimed inventions under Section 102(g)(2). In July 1993, Abbott identified a high affinity antibody to IL-12 as a target for further research. (Pearson Ex. 14, July 30 Memo., at ABT-IL12-00324514-15). On August 25,

[46] Centocor does not address the significance of the amendments to Section 116 that were also part of the 1984 enactments and increased protections for joint inventions. *See* Pub.L. 98-622, Title I, § 104, 98 Stat. 3384 (Nov. 8, 1984). For analysis of the significance of the amendments, see *Kimberly-Clark*, 973 F.2d at 917; *OddzOn Prods. v. Just Toys*, 122 F.3d 1396, 1403 (Fed. Cir. 1997).

1993, Abbott entered into a "collaborative development program" with CAT aimed at isolating "human neutralizing antibodies to certain human antigens." (Oyloe Ex. 52, 1993 Agmt.). In March 1995, the companies agreed to target IL-12 and contracted with GI in that effort, leading to a partnership among the three companies that took effect July 1, 1995. (Oyloe Ex. 53, J. Salfeld Letter; Ex. 54, CAT-GI MTA; Ex. 55, RDMA; Oyloe Ex. 56, Anti-IL-12 Agmt.). Between September 1995 and January 1996, that collaborative effort yielded discoveries of antibodies to IL-12, the Joe antibodies. (Oyloe Ex. 50, Murphy Rpt. ¶¶ 103, 105-06). Further development based on those discoveries produced the inventions disclosed in the '128 and '485 patents. ('128 Patent, at 1; '485 Patent, at 1). No evidence suggests that those patents misidentify the inventors involved in that process. That history shows a process of joint inventorship entirely consistent with Section 116, not a series of inventions by separate entities.

For substantially the same reasons, the Joe antibodies are not prior art under the non-derivation requirement of Section 102(f). "Although derivation and priority of invention are akin in that both focus on inventorship," the requirements of Section 102(f) differ from Section 102(g)(2): under Section 102(f), "the person attacking the patent must establish prior conception of the claimed subject matter [by an inventor other than the patentee] *and* communication of the conception [to the patentee]." *Price v. Symsek*, 988 F.2d 1187, 1190 (Fed. Cir. 1993) (emphasis added). Here, the only evidence on which a claim of derivation might be based is the same as that of Centocor's Section 102(g)(2) claim: that Drs. Salfeld, Tracey, and Banerjee invented the Joe antibodies while working as a separate inventive entity. (Oyloe Ex. 50, Murphy Rpt. ¶¶ 97-104). Because the work of those three Abbott employees did not constitute an invention by a separate inventive entity, Centocor cannot establish invalidity under 35 U.S.C. § 102(f).

Because the undisputed record establishes that the Joe antibodies are not prior art to the patents, summary judgment as to that issue will be granted in favor of Abbott.

2. Stelara

Centocor also seeks a ruling that its own inventions anticipated Abbott's patents under Section 102(g)(2). It contends, first, that all claims asserted against it are anticipated by ustekinumab and, in alternative, that the drug Stelara at least anticipates those claims encompassing pharmaceutical compositions of human IL-12 antibodies.[47]

Generally, a patented invention is presumed to have been invented on the date when the patent application was filed. 1-3 Chisum on Patents § 3.08 ("[T]he date of invention of the applicant or patentee . . . is presumed to be the date he files a complete patent application."). But the filing date is not determinative. *Mahurkar*, 79 F.3d at 1576 ("Section 102(a) explicitly refers to invention dates, not filing dates."). An earlier date of invention may be established by showing that, prior to the filing date, the inventor either reduced the invention to practice or conceived of it and exercised reasonable diligence toward reducing it to practice at a later date. *Id.* at 1577. Establishing an earlier date of priority for these purposes requires only that the inventor demonstrate that he or she reduced to practice at least one embodiment of the claimed invention. *In re Jolley*, 308 F.3d 1317, 1322 (Fed. Cir. 2002). In the context of chemical compounds requiring tests to determine relevant biological properties, reduction to practice of one such embodiment requires its actual construction as well as recognition and appreciation that it works for its intended purpose. *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1332 (Fed.

[47] The "antibody claims" alleged to be anticipated by ustekinumab are claims 1-15, 27-40, and 50-63 of the '128 patent. The "composition claims" alleged to be anticipated by Stelara are claims 64 and 70 of the '128 patent and claims 1-4, 6-11, 15-19, and 24-26 of the '485 patent.

Cir. 2001); *Estee Lauder*, 129 F.3d at 594-95.

The parties agree that Ms. Giles-Komar recognized and appreciated that ustekinumab was a human neutralizing antibody to IL-12 no later than April 30, 1998. (Pearson Ex. 55, Giles-Komar Decl. ¶ 13). For purposes of this motion, the Court will therefore assign Centocor's invention the priority date of April 30, 1998.

Centocor contends that no evidence suggests that Abbott reduced to practice an antibody within the scope of the antibody claims before its presumptive priority date of March 25, 1999, when its provisional patent application was filed. In fact, Abbott offers evidence that it reduced to practice antibodies within the scope of the claims both before March 25, 1999, and before Centocor's asserted priority date of April 30, 1998. The BPAI itself concluded that the Joe antibodies, which are within the scope of some of the antibody claims, were reduced to practice beginning in 1995. (Oyloe Ex. 31, Priority Op. at 89, 98, 102). Centocor's own expert, Mr. Murphy, corroborates those invention dates in his report, stating that Joe 7 and Joe 10 were reduced to practice by September 19, 1995, and that Joe 9 was reduced to practice on or about January 15, 1996. (Oyloe Ex. 50, Murphy Rpt. ¶¶ 105-06, 121-22). Abbott's expert, Ms. Ellis, provides evidence that other antibodies within the scope of the claims were reduced to practice in 1996 and 1997. (Abbott Ex. 118, Ex. C to Ellis Rpt.). This evidence is sufficient to establish a factual dispute as to whether Abbott can claim a priority date that is earlier than Centocor's priority date of April 30, 1998.

With respect to the composition claims, Centocor relies on the fact that one inventor named on those claims, Stuart Friedrich, became an employee of GI no earlier than August 1998 and therefore could not have contributed to Abbott's IL-12 research project before then.

(Pearson Ex. 42, Friedrich Dep. Tr. at 13). Because "[a] person must contribute to the conception of the claimed invention to qualify as a joint inventor," *Vanderbilt Univ. v. ICOS Corp.*, 601 F.3d 1297, 1303 (Fed. Cir. 2010), Centocor asserts that the inclusion of Mr. Friedrich as a joint inventor in the patents proves that conception was not complete before August 1998.

The subsequent addition of Mr. Friedrich does not, however, preclude Abbott from proving an earlier invention date. The Federal Circuit has made clear that proof of priority to a genus claim requires less than what is required to establish adequate written description of that claim (which requires disclosure of a representative number of species within the genus). *In re Zletz*, 893 F.2d 319, 323 (Fed. Cir. 1989) ("Priority as to a genus may indeed be shown by prior invention of a single species . . . but the genus will not be patentable to an applicant unless he has generic support therefor."); *see also In re Stempel*, 44 C.C.P.A. 820, 826 (1957) ("[U]nder the law all the applicant can be required to show is priority with respect to so much of the claimed invention as the [prior art] reference happens to show. When he has done that he has disposed of the reference."). Thus, it is plausible that Abbott invented a species of pharmaceutical composition within the scope of its claims before Centocor's priority date of April 30, 1998, but nevertheless required contributions from Mr. Friedrich after that date in order to establish the patentability of Abbott's genus claims under 35 U.S.C. § 112. The addition of Mr. Friedrich after April 30, 1998, therefore is not conclusive as to the question whether Abbott invented a pharmaceutical composition within the scope of the composition claims before that date.

Additional evidence supports Abbott's assertion that it did in fact invent pharmaceutical compositions of antibodies to IL-12 earlier than April 30, 1998. (Oyloe Exs. 111-15). If that evidence sustains Abbott's claim to priority, but further evidence shows that Mr. Friedrich, after

subsequently joining the research project, made no further contributions, it might suggest that Mr. Friedrich was misjoined as an inventor on the patents. *See, e.g.*, *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1348-49 (Fed. Cir. 1998). However, that possibility does not entitle Centocor to summary judgment on the issue of priority.

In short, because the parties dispute when Abbott reduced to practice inventions within the scope of the antibody and composition claims, summary judgment will be denied.

IV. Infringement

Evaluating an allegation of patent infringement requires a two-step analysis: "the court first determines, as a matter of law, the correct claim scope, and then the fact-finder compares the properly construed claim to the accused device to determine, as a matter of fact, whether all of the claim limitations are present, either literally or by a substantial equivalent, in the accused device." *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1341 (Fed. Cir. 2001).

Here, Abbott asserts a theory of literal infringement. "Literal infringement exists if each of the limitations of the asserted claim(s) read on, that is, are found in, the accused device." *Tate Access Floors, Inc. v. Interface Architectural Res., Inc.*, 279 F.3d 1357, 1366 (Fed. Cir.2002). Thus, for each asserted claim, the patentee must prove that every limitation of that claim is found in the allegedly infringement product. *Oakley, Inc. v. Sunglass Hut Intern.*, 316 F.3d 1331, 1339 (Fed. Cir. 2003); *S. Bravo Systems, Inc. v. Containment Tech. Corp.*, 96 F.3d 1372, 1376 (Fed. Cir. 1996) (requiring proof of infringement by a preponderance of the evidence).

This Court issued a claim construction order on May 5, 2011. Now, at the second step of the infringement analysis, summary judgment is appropriate only if undisputed facts show that Stelara either does or does not meet each limitation of a properly construed claim.

A. "Human Antibody" Claim Limitation

Centocor seeks a ruling that Stelara does not infringe any of the asserted claims.[48] Abbott opposes that motion and has cross-moved for a ruling that Stelara infringes at least those claims characterized by limitations defined by a threshold k_{off} rate constant, as measured by surface plasmon resonance.[49] All claims at issue in the motions include a limitation that the invention be a "human antibody."[50] The motions hinge on the parties' dispute as to whether ustekinumab is a "human antibody" within the meaning of this Court's construction of that term.[51]

The Court has construed "human antibody," to mean "an antibody that is derived from human DNA and not from the DNA of any non-human species." (May 5 Order, at 36). This interpretation is based on a definitional passage in the specification, the last sentence of which provides:

> However, the term "human antibody," as used herein, is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

('128 Patent col. 26 ll. 55-67, col. 27 1-14). Reasoning that this sentence is characterized by

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[48] The asserted claims are claims 1-2, 4-8, 11-13, 27-30, 32, 38, 50-55, 58, 61, 64, and 70 of the '128 patent and claims 1-4, 6-11, 15-19, and 24-26 of the '485 patent.

[49] These "k_{off} claims" are claims 29, 30, 32, and 64 of the '128 patent and claims 1-4, 6-9, 11, 15-19, and 24 of the '485 patent.

[50] For example, claim 1 of the '128 patent claims "[a]n isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with [particular binding properties]." ('128 Patent col. 385 ll. 11-14).

[51] Abbott argues that Centocor cannot deny infringement because it has represented elsewhere that ustekinumab is a human antibody. Centocor responds that multiple other definitions of "human antibodies" are commonly used in the field, and that ustekinumab may be human under those definitions without coming within the scope of the claim construction. Centocor is correct that the applicable definition is that adopted by the Court. *See Rexnord*, 274 F.3d at 1341.

language of exclusion, the Court concluded that "human antibody is defined in terms of derivation—it must have been derived from fully-human sequences, and antibodies that originated in other species are not encompassed by the invention." (May 5 Order, at 41; '128 Patent col. 26 ll. 55-67, col. 27 ll. 1-14). Thus, the Court reasoned, "the better construction of 'human antibody' is one that explicitly limits the term to antibodies derived from human germline sequences . . . ." (May 5 Order, at 41). On the other hand, the definition of "human antibody" adopted by the Court is not limited to antibodies that are encoded entirely by human germline DNA; rather, the Court explained, the term "broadly encompasses human germline sequences that have been altered or mutated in some way." (*Id.* at 40).

Centocor asserts that ustekinumab is not a "human antibody" within the meaning of this construction because the DNA that encodes the antibody is likely to contain nucleotide sequences that were inserted through N-nucleotide addition inside the B cell of a transgenic mouse.[52] It is undisputed that the antibody genes from which the transgenic mouse assembled ustekinumab contained only human germline DNA. (Pearson Ex. 13, Siegel Rebuttal Rpt. ¶¶ 24-27). However, Centocor's expert, Dr. Siegel, asserts that N-nucleotide addition may have occurred during the recombination of those genes inside murine B cells. (*Id.* ¶¶ 13-26). Abbott's expert, Dr. Marks, admits that N-nucleotide addition during that process may have resulted in the addition of nucleotides that are not contained in human germline DNA to the sequences that encode ustekinumab. (Pearson Ex. 16, Marks Dep. Tr. at 116). Thus, the parties do not dispute that ustekinumab is encoded by DNA sequences that contain no germline DNA from any non-

[52] Although the germline sequences may also have been altered by a process called somatic hypermutation, the parties agree that such mutations would not render an antibody not "human." (Oyloe Ex. 4, Siegel Dep. Tr. at 127).

human species, but that do contain human germline DNA together with non-template nucleotides inserted by the cell of a non-human organism (the transgenic mouse). Dr. Siegel asserts that, because the non-template nucleotides originated in the B cell of a non-human organism, ustekinumab is not a "human antibody" under this Court's construction. (Pearson Ex. 13, Siegel Rebuttal Rpt. ¶ 28).

Dr. Siegel's conclusion presupposes that, under the claim construction, DNA introduced through N-nucleotide addition is "DNA of [a] non-human species" within the meaning of the claim construction so long the process occurs inside a cell of a non-human organism. However, this premise does not find express support anywhere in the text of the specification. Nucleotides inserted by N-nucleotide addition are non-template nucleotides, meaning that they are not derived from the germline genomic sequence of any species. (Oyloe Ex. 60, Marks Supp. Rpt. ¶ 9). Whether ustekinumab is a "human antibody" therefore depends whether the term "DNA of any non-human species" includes nucleotides that are not part of the germline DNA of any species but that are assembled and inserted into a DNA sequence inside a cell of a non-human organism.[53]

The Court's construction assumed that the "DNA" that is attributable to a species in this context is the germline DNA of that species. Two considerations make this assumption clear. First, the Court relied on specification language that provided that "human antibody" does not include antibodies for which "sequences derived from the *germline* of another mammalian species . . . have been grafted onto human framework sequences." ('128 Patent col. 26 ll. 55-67, col. 27 1-14). Second, the Court concluded that a proper construction of the term would limit it "to

[53] This question is essentially a legal one because it concerns the interpretation of a term—"DNA of any non-human species"—that is itself part of the adopted claim construction.

antibodies derived from human *germline* sequences." (May 5 Order, at 41). These considerations demonstrate that the adopted construction of "human antibodies" encompassed antibodies encoded by sequences derived from human germline sequences but excluding any non-human germline sequences. The articulation adopted in the Court's order—"an antibody that is derived from human DNA and not from the DNA of any non-human species"—is no different in meaning. Its reference to classes of DNA that are attributable to particular species is synonymous to a reference to the germline sequences of those species.

Under this construction, ustekinumab is a "human antibody" within the meaning of the '128 and '485 patents. The parties' experts, Dr Marks and Dr. Siegel, agree that Stelara was created inside a transgenic mouse through the recombination of human antibody genes together with N-nucleotide additions at the junctions of the recombined sequences. (Marks Supp. Rpt. ¶¶ 35-39; Siegel Rebuttal Rpt. 23-28). The addition of non-template nucleotides during a gene recombination process does not constitute the introduction of "DNA of [a] non-human species." It is simply one manner in which that germline DNA may be "altered or mutated." Dr. Siegel's legal conclusion that the non-template nucleotides added during recombination are "DNA of a non-human species" because they are created by the transgenic mouse B cell is therefore inconsistent with the definition of that term adopted by this Court.

Centocor does not dispute that Stelara meets the remaining limitations of claims 29, 32 and 64 of the '128 patent and claims 1-4, 6-9, 11, 15-19 and 24 of the '485 patent. However, it does offer evidence that ustekinumab does not meet a limitation of claim 30 requiring that the antibody be one that dissociates from IL-12 "with a k_{off} rate constant of 1×10^{-4} s^{-1} or less." (Pearson Ex. 81, at COBI00118796). This dispute of fact precludes summary judgment of

infringement with respect to claim 30.

Accordingly, summary judgment will granted in favor of Abbott on the issue of infringement as to claims 29, 32, and 64 of the '128 patent and claims 1-4, 6-9, 11, 15-19, and 24 of the '485 patent, but denied with respect to the alleged infringement of claim 30 in the '128 patent. Because Centocor's motion relies on a finding that ustekinumab is not a "human antibody," it will be denied.

B. K_d Claim Limitation

Centocor also seeks a ruling that Stelara does not infringe claims that include a limitation defined by a threshold K_d value, as determined by surface plasmon resonance. Using the experimental protocol described in Example 5 in the patent specifications, Centocor's expert, Dr. Robinson, found that ustekinumab did not have a K_d value within the scope of the claims. (Pearson Ex. 5, Robinson Rpt. ¶ 99). Centocor asserts that this result requires summary judgment in its favor. However, at least two factual disputes preclude summary judgment on this issue.[54]

[54] These "K_d claims" are claims 1-15, 27-28, 50-64, and 70 of the '128 patent and claims 11 and 24 of the '485 patent. However, not all of these claims are limited to antibodies that meet their K_d limitations. Claims 11 and 24 of the '485 patent both include a limitation that the claimed antibody "dissociates from the p40 subunit of [an interleukin] with a K_d of 1×10^{-10} M or less or a k_{off} rate constant of 1×10^{-3} s^{-1} or less." ('485 patent col. 382-83). Because these claims use the disjunctive, they encompass antibodies that only meet the k_{off} limitation. Thus, the Court's judgment of infringement with respect to those claims on the basis of k_{off} measurements is not inconsistent with its finding that disputes of fact exist with respect to the K_d value of the ustekinumab's interaction with IL-12 and IL-23.

Claim 64 of the '128 patent is more complicated. It claims "[a] pharmaceutical composition comprising the antibody or an antigen binding portion thereof of claims 1, 16, 21, 27, 29, 41, 44, 45, 48, 50, 51, and a pharmaceutically acceptable carrier." ('128 patent col. 389 ll. 1-4). On its face, this claim appears extremely narrow, as it literally incorporates the limitations of eleven diverse claims in the conjunctive—in other words, all eleven limitations are included. However, Abbott asserts that Stelara is nonetheless within the scope of this claim because it is a pharmaceutical composition comprising the antibody of claim 29 and a pharmaceutically acceptable carrier. Centocor does not dispute that, if Stelara infringes claim 29, then it infringes claim 64. (Centocor Resp. to Statement of Undisputed Facts, at 7). The parties therefore appear to interpret claim 64 to encompass a pharmaceutical composition comprising an antibody of *any one* of the enumerated claims and a pharmaceutically acceptable carrier.

The first relates to experimental methodology. Although Dr. Robinson employed flow rate and RU values provided in Example 5, Abbott's expert, Dr. Myszka, asserts that the example provided protocol for testing an antibody's capacity to bind to an antigen, not for measuring the K_d value of that antibody-antigen interaction. (Oyloe Ex. 37, Myszka Rebuttal Rpt. ¶ 116; '128 Patent col. 117 ll. 7-35). Dr. Myszka also criticizes the methodology of experiments that Dr. Robinson conducted using other protocols. (*Id.*). Whether the methodologies employed by Dr. Robinson were scientifically acceptable is a factual question for the jury.

The second dispute concerns the correct K_d value of the ustekinumab-IL-12 interaction. Abbott's expert, Dr. Rich, measured the K_d of ustekinumab and found that it was within the claimed ranges, contradicting the measurements made by Dr. Robinson. (Oyloe Ex. 70, Rich Rpt. ¶¶ 22-23). Because these experts reached conflicting results, summary judgment is not appropriate on this issue. *See Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1353 (Fed. Cir.1998) ("[D]etermination of infringement, whether literal or under the doctrine of equivalents, is a question of fact").

Accordingly, Centocor's motion for summary judgment as to infringement of the claims that include a limitation defined by a threshold K_d value will be denied.

C. Receptor Binding Assay Claim Limitation

Finally, Centocor also seeks summary judgment that Stelara does not infringe claim 61 of

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In an action for breach of contract or other purely private dispute, the Court would not hesitate to accept the position of the parties notwithstanding its apparent deviation from the text. However, because the patent is a public document with legal implications for parties other than those before the Court in this action, the Court will accept the parties' understanding of scope of claim 64 solely for purposes of this action.

the ’128 patent.[55]

Claim 61 contains a limitation that the claimed antibody must “inhibit[] IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC_{50} of 1×10^{-11} M or less.” (’128 patent col. 388, ll. 64-67). The IL-12 receptor consists of two subunits, called β1 and β2. (Pearson Ex. 29, Marks Rpt. ¶ 24). IL-12 binds to its receptor in such a way that its p40 subunit binds to β1 and its p35 subunit attaches to β2. (*Id.*).[56] Centocor argues that evidence of infringement may consist only of assays that test the ability of an antibody to bind to the IL-12 receptor as a whole—that is, to both subunits simultaneously.

Claim 61 was addressed in the *Markman* proceedings. Centocor proposed a construction limiting the term “receptor binding assay” to assays that use human PHA blasts. In rejecting that interpretation, the Court explained that the plain meaning of the RBA limitation “encompass[es] antibodies tested for IL-12 efficacy using any standard assays known in the art at the time of the invention.” (May 5 Order, at 30).

Abbott’s evidence that ustekinumab infringes claim 61 is based on receptor binding assays conducted by Centocor scientist Dr. Yevgeniya Orlovsky. (Pearson Ex. 29, Marks Rpt. ¶ 60). Dr. Orlovsky tested whether ustekinumab inhibited IL-12 from binding to its β1 receptor subunit by fusing that subunit to a Fc immunoglobulin protein fragment that is not normally present in the IL-12 receptor. (Pearson Ex. 13, Siegel Rebuttal Rpt. ¶¶ 36, 47). Although that experiment did not provide an IC_{50} measurement directly, that value was calculated from the its results. (Pearson

[55] Centocor actually seeks a judgment of noninfringement with respect to claims 61-63 of the ’128 patent. However, Abbott has clarified that it asserts only claim 61 and not claims 62-63. This decision is therefore limited to that claim.

[56] Similarly, IL-23 attaches to a two-part receptor, with its p40 subunit binding to β1 while its p19 subunit binds to a third receptor subunit. (*Id.*).

Ex. 29, Marks. Rpt. ¶ 61; Oyloe Ex. 98, Ralph Rpt. ¶¶ 17-21). According to Dr. Marks, that calculation shows that ustekinumab is within the scope of the RBA limitation of claim 61. (Pearson Ex. 29, Marks. Rpt. ¶ 61).

Centocor argues that infringement cannot be proved in this way because the Orlovsky experiments only tested the ability of ustekinumab to bind to one of the two subparts of the IL-12 receptor (namely, β1). However, the claim construction adopted by this Court allows for proof of inhibition efficacy by "any standard assays known in the art at the time of the invention." Whether the methods used by Dr. Orlovsky were known to those skilled in the art at the time of invention is a factual question. Summary judgment of non-infringement is therefore appropriate only if undisputed evidence shows that his methodologies were not known and accepted in the field at the relevant times as ways to measure IC_{50}.

The record precludes summary judgment on this issue. The parties have offered conflicting expert opinions concerning the probative value of Dr. Orlovsky's experiments. (Pearson Ex. 13, Siegel Rebuttal Rpt. ¶¶ 48-49; Oyloe Ex. 17, Marks Rpt. ¶¶ 60-61; Oyloe Ex. 98, Ralph Rpt. ¶¶ 12-21). Although Dr. Marks testified at his deposition that he was not certain whether a binding assay conducted with β1 alone would be indicative of inhibiting effect on a receptor consisting of both β1 and β2, that testimony alone is not dispositive. (Pearson Ex. 16, Marks. Dep. Tr. at 53-55). Abbott offers other evidence suggesting that the results of those experiments may indicate that ustekinumab inhibits IL-12 from binding from its natural receptor with a particular IC_{50} value. (Oyloe Ex. 78, Marks Dep. Tr. at 50-52; Oyloe Ex. 82, BLA Module 4.2.1.1, at 6; Oyloe Ex. 88, Luo et al., at 798). Faced with this conflicting testimony, this Court is not in a position to declare whether an assay showing that ustekinumab inhibits IL-12 from

binding to one subpart of its receptor is probative of whether the antibody inhibits IL-12 from binding to its receptor as a whole. Weighing the credibility of the experts and the value of their testimony to determine whether the Orlovsky experiments prove infringement of claim 61 is a factual inquiry for the jury. *See TechSearch L.L.C. v. Intel Corp.*, 286 F.3d 1360, 1369 (Fed. Cir. 2002) ("Summary judgment is appropriate when it is apparent that only one conclusion as to infringement could be reached by a reasonable jury.").

Accordingly, Centocor's motion for summary judgment on this issue will be denied.

V. Motion in Limine to Exclude MACE Evidence

Finally, Abbott moves to exclude from trial evidence and testimony relating to Major Adverse Cardiac Events ("MACE") possibly connected to the use of its drug, ABT-874. Both Abbott and Centocor observed a small number of MACE events during clinical trials of their anti-IL-12 antibodies. When they sought FDA approval to sell their drugs, both companies were asked to provide information relevant to MACE events and their drugs. At that point, Abbott withdrew its application for FDA approval. Centocor provided additional information relevant to potential MACE events connected to its product and continued to seek FDA approval. Stelara was subsequently approved for sale in the United States. For the following reasons, the evidence will be admissible, but solely on the issue of damages.

The evidence Abbott seeks to exclude would show the relative incidence of MACE in clinical trials of Stelara and ABT-874. During the placebo-controlled period of the study, Stelara resulted in 1.23 MACE events per 100 patient-years of exposure, while ABT-874 resulted in 1.33 MACE events per 100 patient-years of exposure. Over the period of testing ending with the cut-off day required for regulatory approval, Stelara resulted in .61 MACE events per 100 patient-

years of exposure, while ABT-874 resulted in .60 MACE events per 100 patient-years of exposure. During the cumulative period of clinical study, Stelara resulted in .44 MACE events per 100 patient-years of exposure, while ABT-874 resulted in .52 MACE events per 100 patient-years of exposure. Neither study was designed to evaluate any possible causal connection between the use of the drugs and MACE events, and scientists from both Abbott and Centocor have testified that they do not know of any scientific evidence that there is a connection. (Abbott Ex. B, Weinberg Rebuttal Rpt. ¶ 32; Abbott Ex. E, Valdes Dep. Tr. at 30; Abbott Ex. D, Yeilding Dep. Tr. at 39).

Evidence is generally admissible only if it is relevant. Fed. R. Evid. 402. Evidence is relevant if it has any tendency to make a fact of consequence more or less probable. Fed. R. Evid. 401; *Achille Bayart & Cie v. Crowe*, 238 F.3d 44, 49 (1st Cir. 2001). However, even relevant evidence may be excluded if its probative value is substantially outweighed by a risk of unfair prejudice, confusion, delay, waste of time, or cumulative evidence. Fed. R. Evid. 403. In this action, relevant evidence is limited to that which bears on the validity of the ’128 and ’485 patents, the likelihood that ustekinumab infringes those patents, or the appropriate measure of damages for the alleged infringement.

Centocor first suggests that evidence of MACE events is relevant to whether the patents have adequate written description for the patents’ broad claims. However, written description analysis turns solely on what is claimed and what the disclosures of the specification would tell a person of skill in the art at the time of patent filing. *Ariad,* 598 F.3d at 1350. The genus claimed by the patent encompasses IL-12 antibodies with particular binding properties. Centocor does not explain how the incidence of MACE events is probative as to whether the disclosed antibodies

have those properties and are sufficiently diverse to represent the entire genus of antibodies with those properties. Thus, MACE evidence appears to be irrelevant to this issue.

Centocor's second basis for offering evidence of MACE events relates to damages. Abbott seeks monetary damages of lost profits and a reasonable royalty. Its claim to lost profits relates to sales of its product Humira, not ABT-874, while its royalty claims relate to Centocor's sale of Stelara. MACE events associated with ABT-874, which is contained in neither Humira nor Stelara, are not probative of damages due to lost sales of Humira. However, Abbott's claim to a reasonable royalty is different. It claims damages according to an "entire market value rule" theory premised on the proposition that "the technology of the patents-in-suit drives demand for Stelara." (Centocor Ex. 4, Davis Rpt. at 43). The entire market value rule "allows a patentee to assess damages based on the entire market value of the accused product where the patented feature creates the 'basis for customer demand' or 'substantially create[s] the value of the component parts.'" *Uniloc USA, Inc. v. Microsoft Corp.*, 632 F.3d 1292, 1318 (Fed. Cir. 2011) (quoting *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1336 (Fed. Cir. 2009)). For the rule to apply, "the patentee must prove that the patent-related feature is the basis for customer demand." *Lucent Techs.*, 580 F.3d at 1336. Centocor contends that the fact that Abbott withdrew its FDA application for ABT-874 in response to the agency's inquiry regarding MACE events is evidence that the technology of the patents is not the sole basis of the market demand for Stelara. Put another way, Centocor suggests that the MACE evidence supports an inference that market demand for Stelara is based in part on a perception that it is safe.

Abbott argues that the MACE evidence cannot have any relevance because no evidence suggests a causal connection between the MACE events that occurred during the trials and ABT-

874. That point, however, goes to the probative value of the evidence, rather than its relevance. Even assuming that no causal connection between the use of the drugs and cardiovascular risks can be shown, a difference (even a small one) in the number of MACE events reported in trials of two drugs could conceivably influence public perception of, and therefore market demand for, that drug.

Accordingly, evidence of MACE events will not be admitted insofar as it is offered to prove invalidity or non-infringement, but may be admitted with respect to the proper amount of damages to be awarded if infringement is established.

VI. Conclusion

For the foregoing reasons,

1. Abbott's Motion for Summary Judgment Number 2, that defendants are collaterally estopped from alleging invalidity of U.S. Patent No. 6,914,128, is DENIED;
2. Centocor's Motion for Summary Judgment No. 1, as to noninfringement, or in the alternative, indefiniteness, of the K_d claims, is DENIED;
3. Abbott's Motion for Summary Judgment Number 3, dismissing defendants' claims of indefiniteness of claim limitations relating to surface plasmon resonance, is GRANTED;
4. Centocor's Motion for Summary Judgment No. 7, as to lack of written description of all asserted claims, is DENIED;
5. Centocor's Motion for Summary Judgment No. 3, as to invalidity of the p19 claims for lack of written description, is DENIED;

6. Abbott's Motion for Summary Judgment Number 4, that the named inventors' own work is not "secret prior art," is GRANTED;

7. Centocor's Motion for Summary Judgment No. 5, that the Joe antibodies qualify as prior art, is DENIED;

8. Centocor's Motion for Summary Judgment No. 6, as to anticipation under 35 U.S.C. § 102(g)(2) of all asserted claims and/or anticipation of the composition claims, is DENIED;

9. Abbott's Motion for Summary Judgment Number 1, as to infringement, is GRANTED insofar as the Court finds that Stelara infringes claims 29, 32, and 64 of U.S. Patent No. 6,914,128 and claims 1-4, 6-9, 11, 15-19, and 24 of U.S. Patent No. 7,504,485, and is otherwise DENIED;

10. Centocor's Motion for Summary Judgment No. 2, as to noninfringement of all asserted claims, is DENIED;

11. Centocor's Motion for Summary Judgment No. 4, as to noninfringement of claims 61-63 of the '128 Patent, is DENIED; and

12. Abbott's Motion in Limine to Exclude MACE Evidence is GRANTED in part and DENIED in part as set forth above.

So Ordered.

/s/ F. Dennis Saylor
F. Dennis Saylor IV
United States District Judge

Dated: March 9, 2012